UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

In Re: TAXOTERE (DOCETAXEL) PRODUCTS LIABILITY LITIGATION

MDL NO. 2740

SECTION "N" (5)

THIS DOCUMENT RELATES TO ALL CASES

DEFENDANTS' MOTION TO DISMISS
PLAINTIFFS' MASTER LONG FORM COMPLAINT

NOW INTO COURT, through undersigned counsel, come Defendants, sanofi-aventis U.S. LLC, Sanofi US Services Inc., Sandoz Inc., Hospira, Inc., Hospira Worldwide, LLC, Pfizer Inc., Actavis Pharma, Inc., Accord Healthcare, Inc., Sun Pharma Global Inc.,[1] and McKesson Corporation, which respectfully bring the instant Motion to Dismiss. For the reasons more fully set forth in the attached Memorandum in Support, Defendants move to dismiss Plaintiffs' Master Long Form Complaint pursuant to Federal Rules of Civil Procedure 12(b)(6) and 9(b).

WHEREFORE, Defendants respectfully request that this Court dismiss Plaintiffs' Master Long Form Complaint.

[1] At the time of filing this Motion, Sun Pharma Global Inc. and Plaintiffs have agreed to a voluntary dismissal without prejudice and have further agreed to substitute and accept streamlined service of process for Sun Pharmaceutical Industries, Inc. f/k/a Caraco Laboratories, Ltd. Plaintiffs have also named Sun Pharma Global FZE in this litigation but Sun Pharma Global FZE is a foreign company incorporated under the laws of the United Arab Emirates and has not been served with process, has not agreed to accept service of process in this litigation and consequently, Sun Pharma Global FZE is not appearing in this matter or joining in this Motion.

Respectfully Submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on May 26, 2017, I electronically filed the foregoing with the Clerk of the Court using the ECF system which sent notification of such filing to all counsel of record.

/s/ *Douglas J. Moore*

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

In Re: TAXOTERE (DOCETAXEL) PRODUCTS LIABILITY LITIGATION

MDL NO. 2740

SECTION "N" (5)

THIS DOCUMENT RELATES TO ALL CASES

DEFENDANTS' MEMORANDUM IN SUPPORT OF THEIR MOTION TO DISMISS PLAINTIFFS' MASTER LONG FORM COMPLAINT

Defendants sanofi-aventis U.S. LLC, Sanofi US Services Inc., Sandoz Inc., Hospira, Inc., Hospira Worldwide, LLC, Pfizer Inc., Actavis Pharma, Inc., Accord Healthcare, Inc., Sun Pharma Global Inc.,[1] and McKesson Corporation move to dismiss Plaintiffs' Master Long Form Complaint ("Master Complaint") pursuant to Federal Rules of Civil Procedure 12(b)(6) and 9(b).

I. INTRODUCTION

This product liability action involves an FDA-approved prescription chemotherapy medication known as "Taxotere®" and various other FDA-approved "docetaxel" products (collectively "docetaxel"). Plaintiffs allege that they were prescribed docetaxel by their physicians to treat breast cancer and that they subsequently sustained permanent hair loss.[2] Plaintiffs do not allege that docetaxel was not effective for them. Nor do they claim that Defendants failed to disclose the risk of hair loss, which is a well-known and common side effect

[1] At the time of filing this Motion, Sun Pharma Global Inc. and Plaintiffs have agreed to a voluntary dismissal without prejudice and have further agreed to substitute and accept streamlined service of process for Sun Pharmaceutical Industries, Inc. f/k/a Caraco Laboratories, Ltd. Plaintiffs have also named Sun Pharma Global FZE in this litigation but Sun Pharma Global FZE is a foreign company incorporated under the laws of the United Arab Emirates and has not been served with process, has not agreed to accept service of process in this litigation and consequently, Sun Pharma Global FZE is not appearing in this matter or joining in this Motion.

[2] Plaintiffs define "permanent" alopecia as "an absence of or incomplete hair regrowth six months beyond the completion of chemotherapy." Compl. ¶ 181.

of docetaxel. As Plaintiffs acknowledge, Defendants have included multiple warnings about alopecia in the docetaxel labeling at all pertinent times. *See* Compl. ¶¶ 46, 60, 72, 84, 94, 106, 129. Plaintiffs allege only that they were not told that hair loss might be permanent.

Plaintiffs' Master Complaint asserts eight causes of action against Defendants: (1) strict products liability – failure to warn, (2) strict products liability for misrepresentation, (3) negligence, (4) negligent misrepresentation, (5) fraudulent misrepresentation, (6) fraudulent concealment, (7) fraud and deceit, and (8) breach of express warranty (against sanofi-related entities only). These causes of action are facially deficient as a matter of law, or lack factual allegations sufficient to state a plausible cause of action, or, in some instances, both.

First, the Master Complaint lacks the requisite factual allegations sufficient to state the elements of each claim asserted. Causation, for example, is an essential element of each of Plaintiffs' claims. However, Plaintiffs do not allege that docetaxel itself, or that any alleged failure to warn their physicians about a purported risk of permanent hair loss, actually caused them personal injury. Thus, the Master Complaint should be dismissed because it fails to meet the federal pleading requirements of Rule 8(a)(2) and *Twombly*, obliging Plaintiffs to provide "more than labels and conclusions [because] a formulaic recitation of the elements of a cause of action will not do." *Bell Atl. Corp. v. Twombly*, 550 U.S. 544, 555 (2007).

Second, Plaintiffs' various fraud-based claims must be dismissed under the heightened pleading standard of Rule 9(b), which requires such claims to be pled with particularity. Here, the Master Complaint does not contain a single factual allegation identifying actionable conduct, including any specific event, statement, or conduct by any individual Defendant, when and where the conduct occurred, who engaged in the conduct, to whom it was directed, why it was improper, or how it relates to any alleged injury.

The foundational pleading in a case should not force Defendants and the Court to guess at Plaintiffs' theory of liability or the factual basis of the claims. Before discovery, Defendants have a right to be fairly informed of the specific claims against each of them so that they may ask the appropriate questions at deposition and develop an adequate factual record for any trial.

In MDLs, as in any other case, courts repeatedly hold that "the price of entry, *even to discovery,* is for the plaintiff to allege a *factual* predicate concrete enough to warrant further proceedings, which may be costly and burdensome." *In re Medtronic, Inc. Sprint Fidelis Leads Prods. Liab. Litig.*, No. 08-cv-1905, 2009 WL 294353, at *2 (D. Minn. Feb. 5, 2009) (emphasis in original) (citation omitted), *aff'd* sub nom. 623 F.3d 1200 (8th Cir. 2010). Plaintiffs have failed to adequately plead a viable claim, and they should not be permitted to drag Defendants through a costly and time consuming discovery process.

Accordingly, Defendants respectfully request that this Court grant their motion and dismiss the Master Complaint in its entirety.

II. LEGAL STANDARD

To survive dismissal under Rule 12(b)(6), a "complaint must contain sufficient factual matter, accepted as true, to 'state a claim to relief that is plausible on its face.'" *Ashcroft v. Iqbal*, 556 U.S. 662, 678 (2009) (quoting *Twombly*, 550 U.S. at 570). A claim is facially plausible "when the plaintiff pleads factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." *Id.* However, plausibility requires more than a mere "possibility that a defendant has acted unlawfully." *Id.* Thus, the "[f]actual allegations must be enough to raise a right to relief above the speculative level." *Twombly*, 550 U.S. at 555. A proper pleading "requires more than labels and conclusions," and "[t]hreadbare recitals of the elements of a cause of action, supported by mere conclusory

statements, do not suffice." *Iqbal*, 556 U.S. at 678. Similarly, "naked assertions devoid of further factual enhancement" are insufficient and must be disregarded. *Id.* (internal marks omitted).

Under Rule 9(b), claims for fraud must be pled with particularity. FED. R. CIV. P. 9(b). At a minimum, Rule 9(b) requires the "who, what, when, where, and how" of the alleged fraud. *U.S. ex rel. Thompson v. Columbia/HCA Healthcare Corp.*, 125 F.3d 899, 903 (5th Cir. 1997) (citing *Williams v. WMX Tech., Inc.*, 112 F.3d 175, 179 (5th Cir. 1997)). "The heightened pleading standard for fraud claims supplies defendants with the information they need to prepare responses, prevents discovery intended as a mere fishing expedition, and protects the defendants' reputations from baseless allegations." *U.S. ex rel. Nunnally v. W. Calcasieu Cameron Hosp.*, 519 F. App'x 890, 893 n.2 (5th Cir. 2013); *see also Eckhardt v. Qualitest Pharm., Inc.*, 751 F.3d 674, 681 (5th Cir. 2014) (finding plaintiff failed to allege sufficient facts for his fraud claim to survive in a pharmaceutical product liability case).

MDL courts in this and other circuits also regularly hold plaintiffs to their Rule 9(b) pleading burden for fraud-based causes of action in "master" or "consolidated" complaints. *See, e.g., In re Ford Motor Co. Vehicle Paint Litig.*, No. MDL 1063, 1996 WL 426548 (E.D. La. July 30, 1996) (dismissing fraudulent misrepresentation claim in master complaint for failure to plead reliance); *see also In re McNeil Consumer Healthcare, Mktg. & Sales Practices Litig.*, No. 2:10-md-02190, 2011 WL 2802854 (E.D. Pa. July 15, 2011) (dismissing consolidated complaint for lack of standing and finding fraud claims were not pled with particularity).[3]

[3] *See also In re Ford Motor Co. Speed Control Deactivation Switch Prods. Liab. Litig.*, No. 05-md-01718, 2007 WL 2421480 (E.D. Mich. Aug. 24, 2007); *In re Bridgestone/Firestone, Inc. Prods. Liab. Litig.*, No. 00-ip-9373, 2001 WL 34136021 (S.D. Ind. Sept. 6, 2001); *In re Gen. Motors Corp. Anti-Lock Brake Prods. Liab. Litig.*, 966 F. Supp. 1525, 1535 (E.D. Mo. 1997), *aff'd* sub nom. *Briehl v. Gen. Motors Corp.*, 172 F.3d 623 (8th Cir. 1999);

III. ARGUMENT

SHOTGUN PLEADING

A. Plaintiffs' "Shotgun Pleading" Violates Rule 8 Pleading Standards

Plaintiffs' Master Complaint engages in several types of shotgun pleading in violation of the Federal Rules of Civil Procedure.

First, Plaintiffs' Master Complaint impermissibly incorporates long narrative sections into each cause of action by reference, making it virtually impossible for Defendants to identify what facts are part of which cause of action. *See, e.g.*, *Martin v. Tesoro Corp.*, No. 2:11-cv-1413, 2012 WL 1866841, at *2 (W.D. La. May 21, 2012) ("A shotgun pleading is one that sets forth an excessive number or facts and then asserts in a conclusory fashion that each of those facts supports a number of legal claims, with the result that 'each count is replete with factual allegations that could not possibly be material to that specific count, and that any allegations that are material are buried beneath innumerable pages of rambling irrelevancies.'") (quoting *Magluta v. Samples*, 256 F.3d 1282, 1284 (11th Cir. 2001)). This type of shotgun pleading places a burden on defendants responding to the pleading, and on the court interpreting it. More than two-thirds of Plaintiffs' Master Complaint is devoted to an "extended narrative" describing supposed misconduct by Defendants. Plaintiffs follow this narrative with eight causes of action, formulaically outlining the elements of each claim without the factual support required by federal pleading standards.

Second, Plaintiffs compound this problem by asserting seven of their eight causes of action (all except breach of express warranty) against "All Defendants," collectively. Plaintiffs allege that Defendants communally did or did not do certain things, but they fail to specify what

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In re New England Compounding Pharmacy, Inc. Prods. Liab. Litig., No. 13-02419-RWZ, 2014 WL 4322409 (D. Mass. Aug. 29, 2014).

conduct they allege each Defendant did or did not do. In cases where "geographic and temporal realities make plain that all of the defendants could not have participated in every act complained of," a complaint that references all defendants collectively is an improper "shotgun pleading" because it is impossible for the court, and parties, to determine which defendant allegedly engaged in which acts. *Martin*, 2012 WL 1866841, at *2 (citing *Magluta*, 256 F.3d at 1284). Plaintiffs bear the burden "to provide fair notice of the grounds for the claims made against each of the defendants." *Fox v. Ca. Franchise Tax Bd.*, 443 F. App'x 354, 362 (10th Cir. 2011) (citing *Robbins v. Oklahoma*, 519 F.3d 1242, 1250 (10th Cir. 2008)).

No such notice is provided here. Plaintiffs' negligence claim, for example, alleges a laundry list of purported "acts and/or omissions" by "Defendants, their agents, servants, and/or employees," including generic allegations directed to all Defendants of misconduct related to "manufacturing, producing, promoting, formulating, creating, and/or designing [docetaxel]." Compl. ¶ 243.[4] Similarly, their strict products liability for misrepresentation claim alleges that "Defendants misrepresented facts as set forth herein concerning the character or quality of [docetaxel]" and that "Defendants' misrepresentations were made to potential prescribers and/or purchasers or users of the public at large." *Id.* at ¶¶ 235-36. They do not allege what purported misrepresentation any single Defendant allegedly made to any person at any time.

When, as here, a complaint "use[s] . . . the collective term 'Defendants' . . . with no distinction as to what acts are attributable to whom, it is impossible for any of these individuals to ascertain what particular [] acts they are alleged to have committed." *Fox*, 443 F. App'x at

[4] To the extent Plaintiffs allege a design defect claim, courts have repeatedly held that such claims are preempted. *See, e.g., Yates v. Ortho-McNeil-Janssen Pharm., Inc.*, 808 F.3d 281, 298-99 (6th Cir. 2015); *see also Johnson v. Teva Pharm. USA, Inc.*, 758 F.3d 605, 612-13 (5th Cir. 2014); *Eckhardt*, 751 F.3d at 678-79; *Utts v. Bristol-Myers Squibb Co.*, No. 16-cv-5668, 2016 WL 7429449, at *12 (S.D.N.Y. Dec. 23, 2016); *but see In re Xarelto (Rivaroxaban) Prods. Liab. Litig.*, No. MDL 2592, 2017 WL 1395312, at *3-4 (E.D. La. Apr. 13, 2017) (Fallon, J.). Defendants reserve the right to more fully brief preemption arguments to the extent this litigation proceeds.

362. Because Plaintiffs' pleading does not give Defendants fair notice of the claims against them as required by Rule 8, the Court should dismiss the Master Complaint.

CAUSATION

B. All of Plaintiffs' Claims Must be Dismissed Because Plaintiffs Fail to Allege Causation

Plaintiffs' claims should be dismissed because Plaintiffs do not allege causation, an essential element of each claim. To state a products liability claim based on an alleged personal injury, a plaintiff must plead and prove that the product caused physical harm to the plaintiff and that defendant's alleged misconduct proximately caused plaintiff's alleged injury. *See, e.g.*, RESTATEMENT (SECOND) OF TORTS § 402A(1),[5] 402B, 430, 557A (1965) (causation is an element of claims for strict liability for product defect, strict liability for misrepresentation, negligence, and fraudulent misrepresentation); *Pa. Employees Ben. Trust Fund v. Astrazeneca Pharm. LP*, No. 6:09-cv-5003, 2009 WL 2231686, at *4 (M.D. Fla. July 20, 2009) (express warranty); *Yurcic v. Purdue Pharma, L.P.*, 343 F. Supp. 2d 386, 394 (M.D. Pa. 2004) (same).

Plaintiffs do not even allege that docetaxel caused their alleged permanent hair loss. They allege only that they "are women who were diagnosed with breast cancer, underwent chemotherapy using Taxotere, Docetaxel Injection, Docetaxel Injection Concentrate, and/or Docefrez, and now suffer from permanent hair loss, a side effect for which they were not warned and were wholly unprepared." Compl. ¶ 5; *see also id.* at ¶ 231. Plaintiffs fail to actually allege that absent their use of docetaxel, they would not have experienced permanent hair loss.

[5] Except for the states that have rejected the strict products liability doctrine, each of the states in which Plaintiffs reside evaluate strict liability claims under the framework set forth in Section 402A or substantially equivalent state law. *See, e.g.*, *King v. Danek Med., Inc.*, 37 S.W.3d 429, 435 (Tenn. Ct. App. 2000) ("[Pursuant to the Tennessee Products Liability Act, a] manufacturer or seller of a product shall not be liable for any injury to person . . . caused by the product unless the product is determined to be in a defective condition or unreasonably dangerous at the time it left the control of the manufacturer or seller.") (quoting TENN. CODE ANN. § 29–28–105(a)); *see also Keck v. Dryvit Sys., Inc.*, 830 So.2d 1, 5 (Ala. 2002) ("The [Alabama Extended Manufacturer's Liability Doctrine] is a judicially created accommodation of Alabama law to the doctrine of strict liability for damage or injuries caused by allegedly defective products.") (citation omitted).

Nor is it enough to allege that a manufacturer failed to warn of a particular risk. Rather, a plaintiff must plead and prove that the failure to warn was a "producing cause" of injury. *Ackermann v. Wyeth Pharm.*, 526 F.3d 203, 208 (5th Cir. 2008) (citing *Porterfield v. Ethicon, Inc.*, 183 F.3d 464, 467-68 (5th Cir. 1999)). Here, where the "learned intermediary doctrine" applies, "the manufacturer has no duty to warn the patient, but need only warn the patient's physician." *Willett v. Baxter Int'l, Inc.*, 929 F.2d 1094, 1098 (5th Cir. 1991); *Ackermann*, 526 F.3d at 207-08. A prescription-drug manufacturer "discharge[s] its duty . . . when it has reasonably informed prescribing physicians of the dangers of harm from such a drug." *Anderson v. McNeilab, Inc.*, 831 F.2d 92, 93 (5th Cir. 1987) (citing *Cobb v. Syntex Labs., Inc.*, 444 So.2d 203, 203 (La. Ct. App. 1983)). It follows that causation in this context requires a showing that "a proper warning would have changed the decision of the treating physician, *i.e.*, that but for the inadequate warning, the treating physician would not have used or prescribed the product." *Wheat v. Pfizer, Inc.*, 31 F.3d 340, 343 (5th Cir. 1994) (quoting *Willett*, 929 F.2d at 1099). Among other things, Plaintiffs fail to allege the following:

- That another drug would have successfully treated Plaintiffs' breast cancer;
- That another drug would have been free from all risk of permanent alopecia (to do so would be contrary to scientific fact and resort to total speculation);
- That Plaintiffs' respective prescribing physicians even read the relevant docetaxel labeling;[6] or
- That, had the labeling said something different about alopecia, Plaintiffs' prescribing physicians would have made a different prescribing decision.

Because Plaintiffs do not allege facts sufficient to establish causation, their claims should be dismissed. *See, e.g.*, *Aston v. Johnson & Johnson*, No. 16-cv-0086, 2017 WL 1214399, at *7

[6] While it is possible that Plaintiffs' physicians could have reviewed the docetaxel labeling prior to prescribing the drug to Plaintiffs, a showing that causation is merely possible – as opposed to plausible – is insufficient to sustain Plaintiffs' pleading burden at this stage. *See Ashcroft*, 556 U.S. at 678.

(D.D.C. Mar. 31, 2017) (dismissing failure-to-warn claim for not pleading causation where plaintiffs did not allege "'facts about the timing of [each plaintiff's] use of [the drug], the onset of [their injuries],' . . . . and why they think [the drug] was the cause of these injuries—let alone why they think inadequate *warnings* contributed to their injuries") (first and third alterations in original) (quoting *Salvio v. Amgen, Inc.*, 810 F. Supp. 2d 745, 752 (W.D. Pa. 2011)).

STRICT PRODUCTS LIABILITY FOR MISREPRESENTATION

C. Plaintiffs' Strict Products Liability for Misrepresentation Claim Fails

Plaintiffs' "Strict Products Liability for Misrepresentation" claim should be dismissed for several other, independent reasons. First, many states do not recognize a cause of action based in strict liability for misrepresentation. Since the claim is not common to Plaintiffs, it should not be included in the Master Complaint, which is intended to consist of "common allegations." Compl. ¶¶ 1-2.[7] Second, even in states that do recognize this claim, a plaintiff must allege an express misrepresentation. Omissions alone are insufficient. Here, the Master Complaint asserts that Defendants failed to disclose the alleged risk of permanent alopecia, but it does not, as required, identify any express misrepresentation. Third, as discussed more fully in Section E., *infra*, this cause of action incorporates by reference Plaintiffs' fraud allegations, which Plaintiffs have not pled with the particularity required by Rule 9(b). As a result, Plaintiffs' strict liability for misrepresentation claim fails.

[7] At a minimum, to provide Defendants with fair notice of the claims being asserted, Plaintiffs should list the states for which they believe this cause of action is viable.

1. Plaintiffs' Strict Products Liability for Misrepresentation Claim is Not Actionable in Many States

In addition to the states that do not recognize strict liability causes of action at all,[8] many other states do not recognize a claim for strict products liability based on misrepresentation. For example, there are more than 450 MDL plaintiffs that reside in either Alabama or Louisiana, yet these states do not permit such a claim. *See Barnhill v. Teva Pharm. USA, Inc.*, No. 06-cv-0282, 2007 WL 6947996, at *7 (S.D. Ala. Apr. 24, 2007); *Vitatoe v. Mylan Pharm., Inc.*, 696 F. Supp. 2d 599, 606 (N.D. W.Va. 2010). In *Barnhill*, the plaintiff alleged that she developed Stevens-Johnson-Syndrome after taking a prescription antibiotic. The district court dismissed her claim for "strict liability under § 402B, Restatement (Second) of Torts," explaining that "Alabama has not adopted the no-fault concept embodied in the Restatement but, instead, has retained a negligence-based concept of liability in products liability cases." 2007 WL 6947996 at *7 (citing *Griggs v. Combe, Inc.*, 456 So.2d 790, 792 (Ala. 1984)).

Similarly, in *Vitatoe*, in which plaintiff alleged that her son was injured by a prescription antiepileptic medicine, the court held that under the Louisiana Products Liability Act ("LPLA"), claims for "strict liability, negligence, breach of implied warranty, § 402B misrepresentation, intentional conduct, reckless indifference, and malice, emotional distress, and loss of consortium do not survive." 696 F. Supp. 2d at 606; *see also Jefferson v. Lead Indus. Ass'n, Inc.*, 106 F.3d

[8] For example, North Carolina, Massachusetts, Virginia, and Michigan, among others, do not recognize claims for strict liability. *See* N.C. GEN. STAT. § 99B-1.1 (1996) ("There shall be no strict liability in tort in product liability actions."); *Kelley v. Eli Lilly & Co.*, 517 F. Supp. 2d 99, 109 (D.D.C. 2007) ("[I]n product liability cases, Massachusetts does not have a strict liability tort apart from liability for breach of warranty under the Uniform Commercial Code."); *Sneath v. Conair Corp.*, 35 Va. Cir. 127, 127 (1994) ("Virginia law has not adopted [Section] 402A of the Restatement (Second) of Torts and does not permit tort recovery on a strict-liability theory in products-liability cases."); *Johnson v. Chrysler Corp.*, 254 N.W.2d 569, 571 (Mich. Ct. App. 1977) ("In Michigan, two theories of recovery are recognized in product liability cases; negligence and implied warranty. Strict liability has not been recognized as a third theory of recovery.").

1245, 1251 (5th Cir. 1997) ("A plaintiff may not recover from a manufacturer for damage caused by a product on the basis of any theory of liability not set forth in the LPLA.").

Other states, including New York, Florida, and California, also do not recognize Plaintiffs' claim for strict liability based on misrepresentation. *See, e.g.*, *Hawkins v. Medtronic, Inc.*, 62 F. Supp. 3d 1144, 1162 (E.D. Cal. 2014) (dismissing "strict products liability—misrepresentation" claim because it "no longer appears to be viable under California law"); *DiBartolo v. Abbott Labs.*, 914 F. Supp. 2d 601, 623 (S.D.N.Y. 2012) ("'New York has never adopted the strict liability approach set forth in Section 402B of the Restatement.'") (quoting *Prohaska v. Sofamor, S.N.C.*, 138 F. Supp. 3d 422, 447-48 (W.D.N.Y. 2001)); *Sobkowski v. Wyeth, Inc.*, No. 5:04-cv-96, 2004 WL 3569704, at *6 (M.D. Fla. May 17, 2004) ("[N]o Florida court has ever adopted Restatement (Second) of Torts § 402B."), *report and recommendation adopted as modified*, No. 5:04-cv-96, 2004 WL 3581799 (M.D. Fla. June 24, 2004).

Accordingly, because Plaintiffs' claim does not "generally pertain" to Plaintiffs, the Court should dismiss it.

2. Plaintiffs Have Not Identified an *Express* Misrepresentation as Required for a Strict Products Liability for Misrepresentation Claim

Where states have recognized claims for strict liability for misrepresentation, they have relied on Section 402B of the Restatement (Second) of Torts, which provides:

> One engaged in the business of selling chattels who, by advertising, labels, or otherwise, makes to the public a misrepresentation of a material fact concerning the character or quality of a chattel sold by him is subject to liability for physical harm to a consumer of the chattel caused by justifiable reliance upon the misrepresentation, even though . . . it is not made fraudulently or negligently.

RESTATEMENT (SECOND) OF TORTS § 402B (1965).

Such claims are derived from express warranty claims and require express misrepresentations. *See Am. Safety Equip. Corp. v. Winkler*, 640 P.2d 216, 218-21 (Colo. 1982)

("[T]he rule stated in section 402B stems from the concept of express warranty by advertising."); *accord Baughn v. Honda Motor Co., Ltd.*, 727 P.2d 655, 667 (Wash. 1986). In addition, because Section 402B does not require scienter, courts have held that an express misrepresentation is necessary to prevent the cause of action from becoming a form of absolute liability or displacing other causes of action. *See Franks v. Nat'l Dairy Prods. Corp.*, 282 F. Supp. 528 (W.D. Tex. 1968) *aff'd,* 414 F.2d 682 (5th Cir. 1969); *see also Am. Safety Equip. Corp.*, 640 P.2d at 221 ("Strict tort liability for misrepresentation does not impose an insurer status upon the manufacturer.").

Courts also reject strict liability claims based on implicit misrepresentations. *See Franks*, 282 F. Supp. at 533-34; *English v. Suzuki Motor Co., Ltd.*, 120 F.3d 270 (10th Cir. 1997) (unpublished) (Section 402B requires "an affirmative representation of material fact regarding the character or quality of the product."); *Adkins v. Ford Motor Co.*, 446 F.2d 1105, 1108 (6th Cir. 1971) ("[A]t the least, Tennessee law requires reliance on a particular and specific statement concerning quality or fitness as the foundation for an action of misrepresentation under Section 402B."); *Wolfe v. McNeil-PPC, Inc.*, 773 F. Supp. 2d 561, 573 (E.D. Pa. 2011) (dismissing misrepresentation claim where plaintiff failed "to identify any specific misrepresentation on the labels about the quality of the product itself"); David M. Holliday, American Law of Products Liability § 26:12 (3d ed. 2017) ("Since the rule is concerned with the express misstatement of a material fact by the manufacturer, it does not apply to representations inferred from the nondisclosure of facts, such as the absence of a warning, that allegedly causes injury.").

As demonstrated above, Plaintiffs' strict liability for misrepresentation claim fails to allege an express misrepresentation. Plaintiffs allege only that Defendants omitted a purported risk of permanent alopecia, but that does not amount to an actionable Section 402B claim. To

the extent that Plaintiffs have alleged that "Defendants misrepresented to the public, the FDA, and the medical profession that Taxotere [and docetaxel] are free from permanent side effects," (Compl. ¶ 11), the allegation is implausible. The very labeling on which they rely contains no such statement. Indeed, the labeling for docetaxel has always included warnings about potentially serious risks, including death. *See, e.g.*, Taxotere Label, Dec. 23, 1999 (Ex. A at 1).[9] Thus, Plaintiffs' allegation is not plausible on its face. *See Iqbal*, 556 U.S. at 678.

3. Plaintiffs Have Not Satisfied Rule 9(b) in Pleading a Strict Products Liability for Misrepresentation Claim

As set forth more fully in Section E, *infra*, a heightened pleading standard applies to averments of fraud when used to support non-fraud claims. *See Am. Realty Trust, Inc. v. Travelers Cas. & Sur. Co. of Am.*, 362 F. Supp. 2d 744, 749-51 (N.D. Tex. 2005). Plaintiffs' strict liability for misrepresentation and negligent misrepresentation claims are based on the same common allegations, incorporated by reference, that Defendants made false and misleading statements and omissions. *See, e.g.*, Compl. ¶ 235. But those allegations fail to satisfy Rule 9(b) because Plaintiffs do not identify with particularity to whom, when, or how those statements were made.

If possible, courts should "disregard" or "strip from the claim" improperly pled allegations of fraud, and determine whether remaining non-fraud claims survive under regular pleading standards. *Am. Realty Trust, Inc.*, 362 F. Supp. 2d at 751-52. But if the relevant allegations are intertwined or if a "line-by-line redaction" would be required, dismissal is

[9] The Court may take judicial notice of the Taxotere Label. *See Funk v. Stryker Corp.*, 631 F.3d 777, 783 (5th Cir. 2011) (stating that judicial notice was appropriate for "publicly available documents and transcripts produced by the FDA, which were matters of public record and directly relevant to the issue at hand"); *Pramann v. Janssen Pharm., Inc.*, No. 16-cv-12413, 2017 WL 58469, at *2 (E.D. La. Jan. 5, 2017) (taking judicial notice of "FDA approved Risperidone label" attached to defendant's motion to dismiss); *Cooper v. Pfizer, Inc.*, No. 14-cv-3705, 2015 WL 2341888, at *2 (S.D. Tex. May 13, 2015) (considering "the contents of the FDA approved label" attached to defendant's motion to dismiss); *Elmazouni v. Mylan, Inc.*, No. 16-cv-00574, 2016 WL 7105021, at *3 (N.D. Tex. Dec. 1, 2016) (same).

warranted. *See id.* at 752-53 (dismissing negligent misrepresentation claim where it was not possible to "strip away inadequate allegations of fraud without 'rewrit[ing] . . . [the] deficient complaint'") (quoting *Lone Star Ladies Inv. Club v. Schlotzsky's Inc.*, 238 F.3d 363, 368 (5th Cir. 2001)).

For example, in *Berry v. Indianapolis Life Ins. Co.*, the court dismissed a claim for negligent misrepresentation under Rule 9(b) where plaintiffs "pled negligent misrepresentation as a lesser-included offense to their fraud claims," and "the factual allegations underlying the claims [we]re verbatim." No. 3:08-cv-0248, 2010 WL 3422873, at *14 (N.D. Tex. Aug. 26, 2010). The same analysis applies and warrants dismissal here. As Plaintiffs have made no effort to distinguish which allegations apply to which claims or which Defendants, the Court need not engage in a line-by-line redaction to determine whether the misrepresentation claims survive.

BREACH OF EXPRESS WARRANTY

D. Plaintiffs' Breach of Express Warranty Claim Against the sanofi Defendants Fails

Plaintiffs' breach of express warranty claim is also deficient. First, the sanofi Defendants cannot be liable for any express warranties made by other Defendants. While this cause of action is made only against "Sanofi-Related Entities" it alleges those Defendants made express warranties with regard to docetaxel products not made or sold by sanofi, including "Docefrez, Docetaxel Injection, and Docetaxel Injection Concentrate." Compl. ¶ 313. The sanofi Defendants, however, cannot be held liable for how any product, other than their own, was allegedly "warranted." *See Johnson v. Teva Pharm. USA, Inc.*, 758 F.3d 605, 616 & n.3 (5th Cir. 2014) (finding no liability against a name-brand manufacturer for injuries caused by ingestion of a generic drug under Louisiana law and observing that "[o]ur decision is consistent with other circuit decisions that have held (under the laws of several different states) that brand-name

manufacturers are not liable for injuries caused by a plaintiffs ingestion of generic products"). Thus, any claims regarding alleged express warranties with regard to Docefrez, Docetaxel Injection, and Docetaxel Injection Concentrate must be dismissed.

Second, Plaintiffs' Master Complaint fails to allege facts sufficient to support their claim that the sanofi Defendants breached any alleged express warranties for Taxotere. *See* Compl. ¶¶ 312-319. Plaintiffs formulaically recite the elements of a breach of warranty action, without any factual support. *See id.* at ¶¶ 313-315. Plaintiffs do not identify what or how any information was "expressly warranted" to Plaintiffs or their prescribing physicians. *See Strayhorn v. Wyeth Pharms., Inc.*, 737 F.3d 378, 395 (6th Cir. 2013) (affirming dismissal of express warranty claims where "[t]he plaintiffs' allegations . . . do not identify any affirmation of fact made on the product labeling that they allege to be *false;* rather, they allege that the labeling was *inadequate*"); *Utts*, 2016 WL 7429449, at *13 (dismissing express warranty claim in pharmaceutical failure-to-warn case where "[t]he complaint does not identify the express warranties on which this claim relies, including whether they appeared in the labeling and package inserts for the drug, which were approved by the FDA, whether they appeared in an advertising campaign for the drug, or how the particular warranty was breached"). Like the strict liability for misrepresentation claim, Plaintiffs' breach of express warranty claim requires an express warranty – not simply an alleged omission. Because Plaintiffs do not allege any express statement by sanofi, instead arguing omission of the warning they allege should have been included, this claim must be dismissed. *See Young v. Bristol-Myers Squibb Co.*, No. 4:16-cv-00108, 2017 WL 706320, at *15 n.10 (N.D. Miss. Feb. 22, 2017) ("In reaching this conclusion, the Court notes that, while not raised by the defendants, [the plaintiff's] breach of express warranty claim must fail to the extent it is based on alleged omissions in [the defendant's]

prescribing information. An omission is neither an affirmation of fact nor a promise. *See generally Sidco Prods. Mktg. v. Gulf Oil Corp.*, 858 F.2d 1095, 1099 (5th Cir. 1988) ('Omissions, however, are not affirmative representations of any sort and thus cannot support a warranty claim, because express warranties must be explicit.') (applying Texas law)."); *see also Strayhorn*, 737 F.3d at 395 (holding "express-warranty claims are without merit because the labels never explicitly warranted that metoclopramide was safe for long-term use").

Finally, even if an express warranty existed (it did not), Plaintiffs do not identify how they or their prescribing physicians supposedly relied on any express warranty. This Court is not bound to accept legal conclusions couched as factual allegations as true. *Iqbal*, 556 U.S. at 678. Rule 8 "demands more than an unadorned, the-defendant-unlawfully-harmed-me accusation." *Gulf Coast Hotel-Motel Ass'n v. Miss. Gulf Coast Golf Course Ass'n*, 658 F.3d 500, 504 (5th Cir. 2011) (citing *Iqbal*, 556 U.S. at 678). Therefore, Plaintiffs' breach of express warranty claim must be dismissed for failure to state a claim. *See, e.g., Parra v. Coloplast Corp.*, No. 16-cv-14696, 2017 WL 24794, at *5 (E.D. La. Jan. 3, 2017); *Yurcic v. Purdue Pharma, L.P.*, 343 F. Supp. 2d 386, 394-95 (M.D. Pa. 2004).

FRAUD

E. Plaintiffs' Fraud Claims Fail to Meet the Requisite Pleading Standard

1. Rule 9(b) Applies to Plaintiffs' Claims for Strict Products Liability for Misrepresentation, Negligent Misrepresentation, Fraudulent Misrepresentation, Fraudulent Concealment, and Fraud and Deceit

Plaintiffs' Master Complaint includes five claims premised on alleged misrepresentations: strict products liability-misrepresentation, negligent misrepresentation, fraudulent misrepresentation, fraudulent concealment, and fraud and deceit. These claims must satisfy Rule 9(b). All of these claims are premised on the assertion that Defendants made false and misleading statements and omissions. *See, e.g.*, Compl. ¶¶ 235, 254, 261, 268, 278.

Because these claims allege knowing conduct, they sound in fraud and must satisfy Rule 9(b). *See Benchmark Elec., Inc. v. J.M. Huber Corp.*, 343 F.3d 719, 723 (5th Cir. 2003), *opinion modified on denial of reh'g,* 355 F.3d 356 (5th Cir. 2003); *Lone Star Ladies Inv. Club*, 238 F. 3d at 368 ("Rule 9(b) applies by its plain language to all averments of fraud, whether they are part of a claim of fraud or not."); *In re Ford Motor Co. Vehicle Paint Litig.*, 1996 WL 426548, at *29 (holding plaintiffs failed to plead fraudulent concealment claim with sufficient particularly required by Rule 9(b)); *see also Hawkins v. Medtronic, Inc.*, No. 1:13-cv-00499, 2014 WL 346622, at *17 (E.D. Cal. Jan. 30, 2014) (dismissing strict liability for misrepresentation claim for failing to satisfy Rule 9(b)).

2. Plaintiffs' Conclusory Fraud-Based Allegations Do Not Satisfy Rule 9(b)'s Heightened Pleading Requirements

As Plaintiffs fail even to plead facts sufficient to meet the basic plausibility pleading standard under Rule 8(a)(2), their fraud-based claims fall that much further short of satisfying the heightened standard required by Rule 9(b) and must be dismissed.

Rule 9(b) is only satisfied if the plaintiff supplies "the particulars of time, place, and contents of the false representations, as well as the identity of the person making the misrepresentation and what that person obtained thereby, otherwise referred to as the who, what, when, where, and how of the alleged fraud." *U.S. ex rel. Willard v. Humana Health Plan of Tex., Inc.*, 336 F.3d 375, 384 (5th Cir. 2003) (internal citations and quotation marks omitted). Rule 9(b) is designed "to preclude litigants from filing baseless complaints and then attempting to discover unknown wrongs." *Shushany v. Allwaste, Inc.*, 992 F.2d 517, 521 (5th Cir. 1993) (citing *Guidry v. Bank of LaPlace* ("*Guidry I*"), 740 F. Supp. 1208, 1216 (E.D. La. 1990)); *see also House v. Bristol-Myers Squibb Co.*, No. 3:15-cv-00894, 2017 WL 55876, at *9 (W.D. Ky.

Jan. 4, 2017) (applying Rule 9(b) heightened pleading requirements to fraud claims made in personal injury action involving prescription medications).

Plaintiffs allege no factual basis for their fraud claims, but rather assert only general allegations that Defendants made representations about docetaxel through marketing or labeling. *See* Compl. ¶ 260 ("Defendants represented to Plaintiffs . . . that [the products at issue] had been tested and [were] found to be safe and effective . . ."); *id.* at ¶ 268 ("Defendants misrepresented the design characteristics and safety of [the products at issue] for their intended use."); *id.* at ¶ 279 ("Defendants fraudulently claimed superior efficacy over other products designed to treat the same conditions for which Taxotere was designed to treat.").

But Plaintiffs do not identify with particularity what, to whom, when, or how these representations were made or specify which Defendant or Defendants made them, even though a plaintiff "must allege specific facts supporting an inference of fraud." *Dorsey v. Portfolio Equities, Inc.*, 540 F. 3d 333, 339 (5th Cir. 2008). The Fifth Circuit "interprets Rule 9(b) strictly," and, in order to avoid dismissal, a plaintiff must "specify the statements contended to be fraudulent, identify the speaker, state when and where the statements were made, and explain why the statements were fraudulent." *Id.*; *see also Eckhardt*, 751 F.3d at 681 (finding plaintiff failed to allege sufficient facts for his fraud claim to survive in a pharmaceutical product liability case). Plaintiffs have alleged none of the specific facts required, only claiming that the unspecified representations were "material and false." Compl. ¶ 162. This is not enough to satisfy Rule 9(b). *See Lovelace v. Software Spectrum Inc.*, 78 F.3d 1015, 1019 (5th Cir. 1996).

For all of these reasons, Plaintiffs' claims for strict liability for misrepresentation, negligent misrepresentation, fraudulent misrepresentation, fraudulent concealment, and fraud and deceit should be dismissed.

IV. CONCLUSION

For the reasons mentioned above, Defendants request that this Court grant their Motion to Dismiss Plaintiffs' Master Long Form Complaint.

Respectfully Submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on May 26, 2017, I electronically filed the foregoing with the Clerk of the Court using the ECF system which sent notification of such filing to all counsel of record.

/s/ *Douglas J. Moore*

EXHIBIT A

IN-XXXX Rev. mm/yy

Rx only

TAXOTERE®
(docetaxel)

for Injection Concentrate

WARNING

TAXOTERE® (docetaxel) for Injection Concentrate should be administered under the supervision of a qualified physician experienced in the use of antineoplastic agents. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

The incidence of treatment-related mortality associated with TAXOTERE therapy is increased in patients with abnormal liver function , in patients receiving higher doses, and in patients with non-small cell lung carcinoma and a history of prior treatment with platinum-based chemotherapy who receive TAXOTERE at a dose of 100 mg/m^2 (see **WARNINGS**).

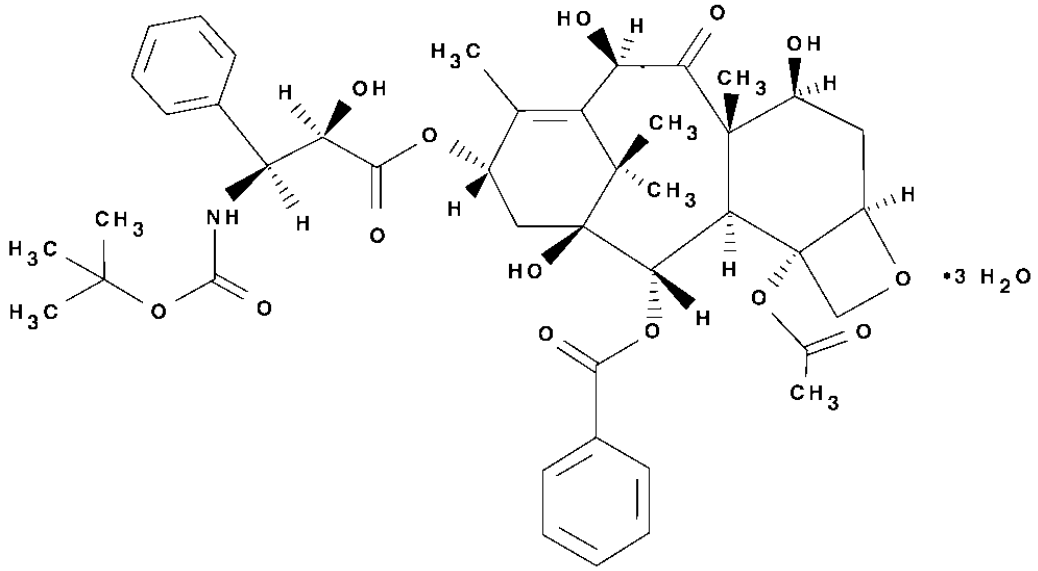
TAXOTERE should generally not be given to patients with bilirubin > upper limit of normal (ULN), or to patients with SGOT and/or SGPT >1.5 x ULN concomitant with alkaline phosphatase > 2.5 x ULN. Patients with elevations of bilirubin or abnormalities of transaminase concurrent with alkaline phosphatase are at increased risk for the development of grade 4 neutropenia, febrile neutropenia, infections, severe thrombocytopenia, severe stomatitis, severe skin toxicity, and toxic death. Patients with isolated elevations of transaminase > 1.5 x ULN also had a higher rate of febrile neutropenia grade 4 but did not have an increased incidence of toxic death. Bilirubin, SGOT or SGPT, and alkaline phosphatase values should be obtained prior to each cycle of TAXOTERE therapy and reviewed by the treating physician.

TAXOTERE therapy should not be given to patients with neutrophil counts of < 1500 cells/mm^3. In order to monitor the occurrence of neutropenia, which may be severe and result in infection, frequent blood cell counts should be performed on all patients receiving TAXOTERE.

Severe hypersensitivity reactions characterized by hypotension and/or bronchospasm, or generalized rash/erythema occurred in 2.2% (2/92) of patients who received the recommended 3-day dexamethasone premedication. Hypersensitivity reactions requiring discontinuation of the TAXOTERE infusion were reported in five patients who did not receive premedication. These reactions resolved after discontinuation of the infusion and the administration of appropriate therapy. TAXOTERE must not be given to patients who have a history of severe hypersensitivity reactions to TAXOTERE or to other drugs formulated with polysorbate 80 (see **WARNINGS**).
Severe fluid retention occurred in 6.5% (6/92) of patients despite use of a 3-day dexamethasone premedication regimen. It was characterized by one or more of the following events: poorly tolerated peripheral edema, generalized edema, pleural effusion requiring urgent drainage, dyspnea at rest, cardiac tamponade, or pronounced abdominal distention (due to ascites) (see **PRECAUTIONS**).

DESCRIPTION

Docetaxel is an antineoplastic agent belonging to the taxoid family. It is prepared by semisynthesis beginning with a precursor extracted from the renewable needle biomass of yew plants. The chemical name for docetaxel is (2R,3S)-N-carboxy-3-phenylisoserine,N-*tert*-butyl ester, 13-ester with 5β-20-epoxy-1,2α,4,7β,10β,13α-hexahydroxytax-11-en-9-one 4-acetate 2-benzoate, trihydrate. Docetaxel has the following structural formula:



Docetaxel is a white to almost-white powder with an empirical formula of $C_{43}H_{53}NO_{14}\bullet 3H_2O$, and a molecular weight of 861.9. It is highly lipophilic and practically insoluble in water. TAXOTERE (docetaxel) for Injection Concentrate is a clear yellow to brownish-yellow viscous solution. TAXOTERE is sterile, non-pyrogenic, and is available in single-dose vials containing 20 mg (0.5 mL) or 80 mg (2.0 mL) docetaxel (anhydrous). Each mL contains 40 mg docetaxel (anhydrous) and 1040 mg polysorbate 80.

TAXOTERE for Injection Concentrate requires dilution prior to use. A sterile, non-pyrogenic, single-dose diluent is supplied for that purpose. The diluent for TAXOTERE contains 13% ethanol in Water for Injection, and is supplied in 1.5 mL (to be used with 20 mg TAXOTERE for Injection Concentrate) and 6.0 mL (to be used with 80 mg TAXOTERE for Injection Concentrate) vials.

CLINICAL PHARMACOLOGY

Docetaxel is an antineoplastic agent that acts by disrupting the microtubular network in cells that is essential for mitotic and interphase cellular functions. Docetaxel binds to free tubulin and promotes the assembly of tubulin into stable microtubules while simultaneously inhibiting their disassembly. This leads to the production of microtubule bundles without normal function and to the stabilization of microtubules, which results in the inhibition of mitosis in cells. Docetaxel's binding to microtubules does not alter the number of protofilaments in the bound microtubules, a feature which differs from most spindle poisons currently in clinical use.

HUMAN PHARMACOKINETICS

The pharmacokinetics of docetaxel have been evaluated in cancer patients after administration of 20-115 mg/m^2 in phase I studies. The area under the curve (AUC) was dose proportional following doses of 70-115 mg/m^2 with infusion times of 1 to 2 hours. Docetaxel's pharmacokinetic profile is consistent with a three-compartment pharmacokinetic model, with half-lives for the α, β, and γ phases of 4 min, 36 min, and 11.1 hr, respectively. The initial rapid decline represents distribution to the peripheral compartments and the late (terminal) phase is due, in part, to a relatively slow efflux of docetaxel from the peripheral compartment. Mean values for total body clearance and steady state volume of distribution were 21 L/h/m^2 and 113 L, respectively. Mean total body clearance for Japanese patients dosed at the range of 10-90 mg/m^2 was similar to that of European/American populations dosed at 100 mg/m^2, suggesting no significant difference in the elimination of docetaxel in the two populations.

A study of ^{14}C-docetaxel was conducted in three cancer patients. Docetaxel was eliminated in both the urine and feces following oxidative metabolism of the *tert*-butyl ester group, but fecal excretion was the main elimination route. Within 7 days, urinary and fecal excretion accounted for approximately 6% and 75% of the administered radioactivity, respectively. About 80% of the radioactivity recovered in feces is excreted during the first 48 hours as 1 major and 3 minor metabolites with very small amounts (less than 8%) of unchanged drug.

A population pharmacokinetic analysis was carried out after TAXOTERE treatment of 535 patients dosed at 100 mg/m^2. Pharmacokinetic parameters estimated by this analysis were very close to those estimated from phase I studies. The pharmacokinetics of docetaxel were not influenced by age or gender and docetaxel total body clearance was not modified by pretreatment with dexamethasone. In patients with clinical chemistry data suggestive of mild to moderate liver function impairment (SGOT and/or SGPT >1.5 times the upper limit of normal [ULN] concomitant with alkaline phosphatase >2.5 times ULN), total body clearance was lowered by an average of 27%, resulting in a 38% increase in systemic

exposure (AUC). This average, however, includes a substantial range and there is, at present, no measurement that would allow recommendation for dose adjustment in such patients. Patients with combined abnormalities of transaminase and alkaline phosphatase should, in general, not be treated with TAXOTERE.

In vitro studies showed that docetaxel is about 94% protein bound, mainly to α_1-acid glycoprotein, albumin, and lipoproteins. In three cancer patients, the *in vitro* binding to plasma proteins was found to be approximately 97%. Dexamethasone does not affect the protein binding of docetaxel.

In vitro drug interaction studies revealed that docetaxel is metabolized by the CYP3A4 isoenzyme, and its metabolism can be inhibited by CYP3A4 inhibitors, such as ketoconazole, erythromycin, troleandomycin, and nifedipine. Based on *in vitro* findings, it is likely that CYP3A4 inhibitors and/or substrates may lead to substantial increases in docetaxel blood concentrations. No clinical studies have been performed to evaluate this finding (see PRECAUTIONS).

CLINICAL STUDIES

Breast Cancer: The efficacy and safety of TAXOTERE have been evaluated in locally advanced or metastatic breast cancer after failure of previous chemotherapy (alkylating agent-containing regimens or anthracycline-containing regimens), primarily at a dose of 100 mg/m^2 given as a 1-hour infusion every 3 weeks, but with some experience at 60 mg/m^2, in two large randomized trials and a number of smaller single arm studies.

Randomized Trials: In one randomized trial, patients with a history of prior treatment with an anthracycline-containing regimen were assigned to treatment with TAXOTERE or the combination of mitomycin (12 mg/m^2 every 6 weeks) and vinblastine (6 mg/m^2 every 3 weeks). 203 patients were randomized to TAXOTERE and 189 to the comparator arm. Most patients had received prior chemotherapy for metastatic disease; only 27 patients on the TAXOTERE arm and 33 patients on the comparator arm entered the study following relapse after adjuvant therapy. Three-quarters of patients had measurable, visceral metastases. The primary endpoint was time to progression. The following table summarizes the study results:

Efficacy of TAXOTERE in the Treatment of Breast Cancer Patients Previously Treated with an Anthracycline-Containing Regimen (Intent-to-Treat Analysis)

Efficacy Parameter	Docetaxel	Mitomycin/ Vinblastine	p-value
	(N=203)	(N=189)	
Median Survival	11.4 months	8.7 months	
Risk Ratio*, Mortality			
(Docetaxel:Control)	0.73		p=0.01
			Log Rank

95% CI (Risk Ratio)	0.58-0.93		
Median Time to Progression	4.3 months	2.5 months	
Risk Ratio*, Progression (Docetaxel:Control)	0.75		p=0.01 Log Rank
95% CI (Risk Factor)	0.61-0.94		
Overall Response Rate	28.1%	9.5%	p<0.0001
Complete Response Rate	3.4%	1.6%	Chi Square

*For the risk ratio, a value less than 1.00 favors docetaxel.

In a second randomized trial, patients previously treated with an alkylating-containing regimen were assigned to treatment with TAXOTERE or doxorubicin (75 mg/m^2 every 3 weeks). 161 patients were randomized to TAXOTERE and 165 patients to doxorubicin. Approximately one-half of patients had received prior chemotherapy for metastatic disease, and one-half entered the study following relapse after adjuvant therapy. Three-quarters of patients had measurable, visceral metastases. The primary endpoint was time to progression. The study results are summarized below:

Efficacy of TAXOTERE in the Treatment of Breast Cancer Patients Previously Treated with an Alkylating-Containing Regimen (Intent-to-Treat Analysis)

Efficacy Parameter	**Docetaxel**	**Doxorubicin**	**p-value**
	(N=161)	**(165)**	
Median Survival	14.7 months	14.3 months	
Risk Ratio*, Mortality			
(Docetaxel:Control)	0.89		p=0.39
			Log Rank
95% CI (Risk Ratio)	0.68-1.16		
Median Time to Progression	6.5 months	5.3 months	
Risk Ratio*, Progression (Docetaxel:Control)	0.93		p=0.45 Log Rank
95% CI (Risk Ratio)	0.71-1.16		
Overall Response Rate	45.3%	29.7%	p=0.004
Complete Response Rate	6.8%	4.2%	Chi Square

*For the risk ratio, a value less than 1.00 favors docetaxel.

Single Arm Studies: TAXOTERE at a dose of 100 mg/m^2 was studied in six single arm studies involving a total of 309 patients with metastatic breast cancer in whom previous chemotherapy had failed. Among these, 190 patients had anthracycline-resistant breast

cancer, defined as progression during an anthracycline-containing chemotherapy regimen for metastatic disease, or relapse during an anthracycline-containing adjuvant regimen. In anthracycline-resistant patients, the overall response rate was 37.9% (72/190; 95% C.I.: 31.0-44.8) and the complete response rate was 2.1%.

TAXOTERE was also studied in three single arm Japanese studies at a dose of 60 mg/m^2, in 174 patients who had received prior chemotherapy for locally advanced or metastatic breast cancer. Among 26 patients whose best response to an anthracycline had been progression, the response rate was 34.6% (95% C.I.: 17.2-55.7), similar to the response rate in single arm studies of 100 mg/m^2.

Hematologic and Other Toxicity: Relation to dose and baseline liver chemistry abnormalities. Hematologic and other toxicity is increased at higher doses and in patients with elevated baseline liver function tests (LFTs). In the following tables, adverse drug reactions are compared for three populations: 730 patients with normal LFTs given TAXOTERE at 100 mg/m^2 in the randomized and single arm studies of metastatic breast cancer after failure of previous chemotherapy; 18 patients in these studies who had abnormal baseline LFTs (defined as SGOT and/or SGPT > 1.5 times ULN concurrent with alkaline phosphatase > 2.5 times ULN); and 174 patients in Japanese studies given TAXOTERE at 60 mg/m^2 who had normal LFTs.

Hematologic Adverse Events in Breast Cancer Patients Previously Treated with Chemotherapy

Treated at TAXOTERE 100 mg/m^2 with Normal or Elevated Liver Function Tests or 60 mg/m^2 with Normal Liver Function Tests

	TAXOTERE 100 mg/m^2		TAXOTERE 60 mg/m^2
	Normal LFTs*	Elevated LFTs**	Normal LFTs*
Adverse Event	n=730	n=18	n=174
	%	%	%
Neutropenia			
Any <2000 cells/mm^3	98.4	100	95.4
Grade 4 <500 cells/mm^3	84.4	93.8	74.9
Thrombocytopenia			
Any <100,000 cells/mm^3	10.8	44.4	14.4
Grade 4 <20,000 cells/mm^3	0.6	16.7	1.1
Anemia <11 g/dL	94.6	94.4	64.9
Infection***			
Any	22.5	38.9	1.1
Grade 3 and 4	7.1	33.3	0
Febrile Neutropenia****			
By Patient	11.8	33.3	0
By Course	2.4	8.6	0

Septic Death	1.5	5.6	1.1
Non-Septic Death	1.1	11.1	0

***Normal Baseline LFTs: Transaminases ≤ 1.5 times ULN or alkaline phosphatase ≤ 2.5 times ULN or isolated elevations of transaminases or alkaline phosphatase up to 5 times ULN**

****Elevated Baseline LFTs: SGOT and/or SGPT >1.5 times ULN concurrent with alkaline phosphatase >2.5 times ULN**

*****Incidence of infection requiring hospitalization and/or intravenous antibiotics was 8.5% (n=62) among the 730 patients with normal LFTs at baseline; 7 patients had concurrent grade 3 neutropenia, and 46 patients had grade 4 neutropenia.**

******Febrile Neutropenia: For 100 mg/m^2, ANC grade 4 and fever > 38° C with IV antibiotics and/or hospitalization; for 60 mg/m^2, ANC grade 3/4 and fever > 38.1° C**

Non-Hematologic Adverse Events in Breast Cancer Patients Previously Treated with Chemotherapy Treated at TAXOTERE 100 mg/m^2 with Normal or Elevated Liver Function Tests or 60 mg/m^2 with Normal Liver Function Tests

Adverse Event	TAXOTERE 100 mg/m^2		TAXOTERE 60 mg/m^2
	Normal LFTs* n=730 %	Elevated LFTs** n=18 %	Normal LFTs* n=174 %
Acute Hypersensitivity Reaction Regardless of Premedication			
Any	13.0	5.6	0.6
Severe	1.2	0	0
Fluid Retention*** Regardless of Premedication			
Any	56.2	61.1	12.6
Severe	7.9	16.7	0
Neurosensory			
Any	56.8	50	19.5
Severe	5.8	0	0
Myalgia	22.7	33.3	3.4
Cutaneous			
Any	44.8	61.1	30.5
Severe	4.8	16.7	0
Asthenia			
Any	65.2	44.4	65.5
Severe	16.6	22.2	0
Diarrhea			
Any	42.2	27.8	NA
Severe	6.3	11.1	
Stomatitis			
Any	53.3	66.7	19.0
Severe	7.8	38.9	0.6

***Normal Baseline LFTs: Transaminases ≤ 1.5 times ULN or alkaline phosphatase ≤ 2.5 times ULN or isolated elevations of transaminases or alkaline phosphatase up to 5 times ULN**

**** Elevated Baseline Liver Function: SGOT and/or SGPT >1.5 times ULN concurrent with alkaline phosphatase >2.5 times ULN**

*****Fluid Retention includes (by COSTART): edema (peripheral, localized, generalized, lymphedema, pulmonary edema, and edema otherwise not specified) and effusion (pleural, pericardial, and ascites); no premedication given with the 60 mg/m^2 dose**

NA = not available

Non-Small Cell Lung Cancer (NSCLC):

The efficacy and safety of TAXOTERE in non-small cell lung cancer have been evaluated in patients with locally advanced or metastatic disease and a history of prior treatment with a platinum-based chemotherapy regimen. Two randomized, controlled trials established that a TAXOTERE dose of 75 mg/m^2 was tolerable and yielded a favorable outcome (see below). TAXOTERE at a dose of 100 mg/m^2, however, was associated with unacceptable hematologic toxicity, infections, and treatment-related mortality and this dose should not be used (see BOXED WARNING, WARNINGS, and DOSAGE AND ADMINISTRATION sections).

One trial (TAX317), randomized patients with locally advanced or metastatic non-small cell lung cancer, a history of prior platinum-based chemotherapy, no history of taxane exposure, and an ECOG performance status ≤2 to TAXOTERE or best supportive care. The primary endpoint of the study was survival. Patients were initially randomized to TAXOTERE 100 mg/m^2 or best supportive care, but early toxic deaths at this dose led to a dose reduction to TAXOTERE 75 mg/m^2. A total of 104 patients were randomized in this amended study to either TAXOTERE 75 mg/m^2 or best supportive care.

In a second randomized trial (TAX320), 373 patients with locally advanced or metastatic non-small cell lung cancer, a history of prior platinum-based chemotherapy, and an ECOG performance status ≤2 were randomized to TAXOTERE 75 mg/m^2, TAXOTERE 100 mg/m^2 and a treatment in which the investigator chose either vinorelbine 30 mg/m^2 days 1, 8, and 15 repeated every 3 weeks **or** ifosfamide 2 g/m^2 days 1-3 repeated every 3 weeks. Forty percent of the patients in this study had a history of prior paclitaxel exposure. The primary endpoint was survival in both trials. The efficacy data for the TAXOTERE 75 mg/m^2 arm and the comparator arms are summarized in the table below and in figures 1 and 2 showing the survival curves for the two studies.

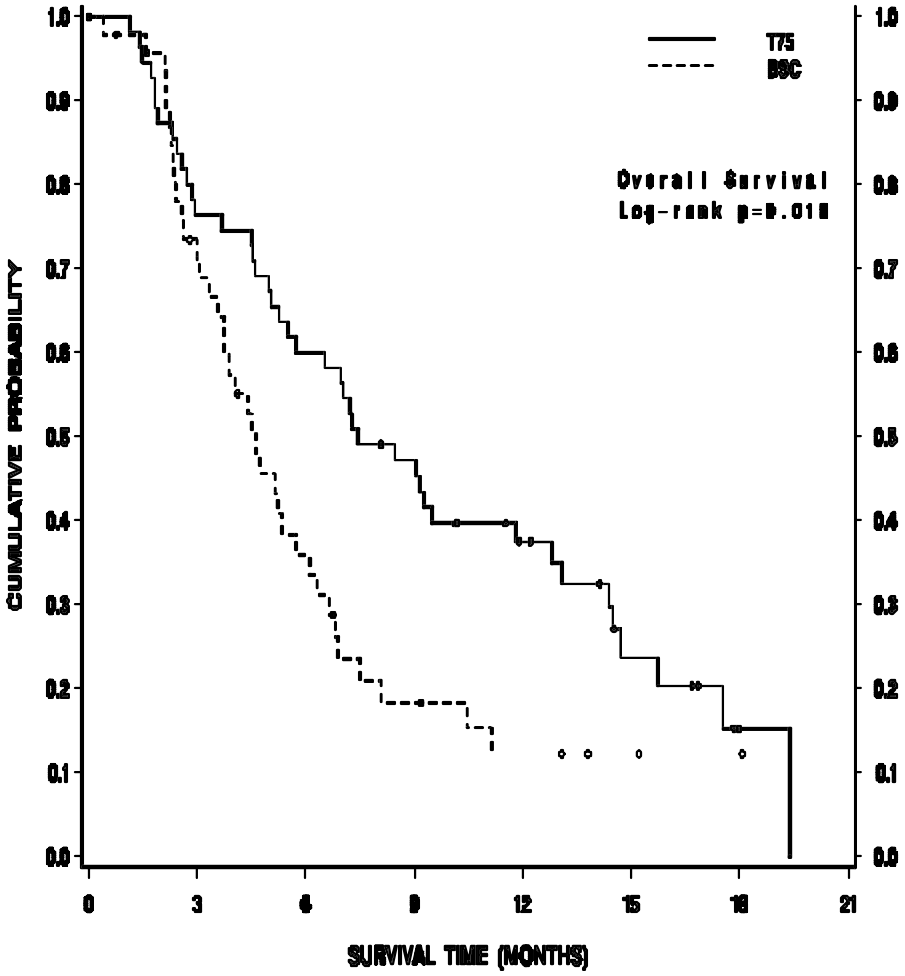
Efficacy of TAXOTERE in the Treatment of Non-Small Cell Lung Cancer Patients Previously Treated with a Platinum-Based Chemotherapy Regimen (Intent-to-Treat Analysis)

	TAX317		TAX 320	
	Docetaxel 75 mg/m^2 N = 55	**Best Supportive Care/75 N = 49**	**Docetaxel 75 mg/m^2 N=125**	**Control (V/I) N= 123**
Overall Survival Log-rank Test	p = 0.01		p = 0.13	
Risk Ratio[#], Mortality (Docetaxel:Control)	0.56		0.82	
95% CI (Risk Ratio)	(0.35, 0.88)		(0.63, 1.06)	
Median Survival	7.5 months*	4.6 months	5.7 months	5.6 months
95% CI	(5.5, 12.8)	(3.7, 6.1)	(5.1, 7.1)	(4.4, 7.9)
% 1-year Survival	37%*[@]	12%	30%*[@]	20%
95% CI	(24, 50)	(2, 23)	(22, 39)	(13, 27)
Time to Progression	12.3 weeks*	7.0 weeks	8.3 weeks	7.6 weeks
95% CI	(9.0, 18.3)	(6.0, 9.3)	(7.0, 11.7)	(6.7, 10.1)
Response Rate	5.5%	Not Applicable	5.7%	0.8%
95% CI	(1.1, 15.1))		(2.3, 11.3)	(0.0, 4.5)

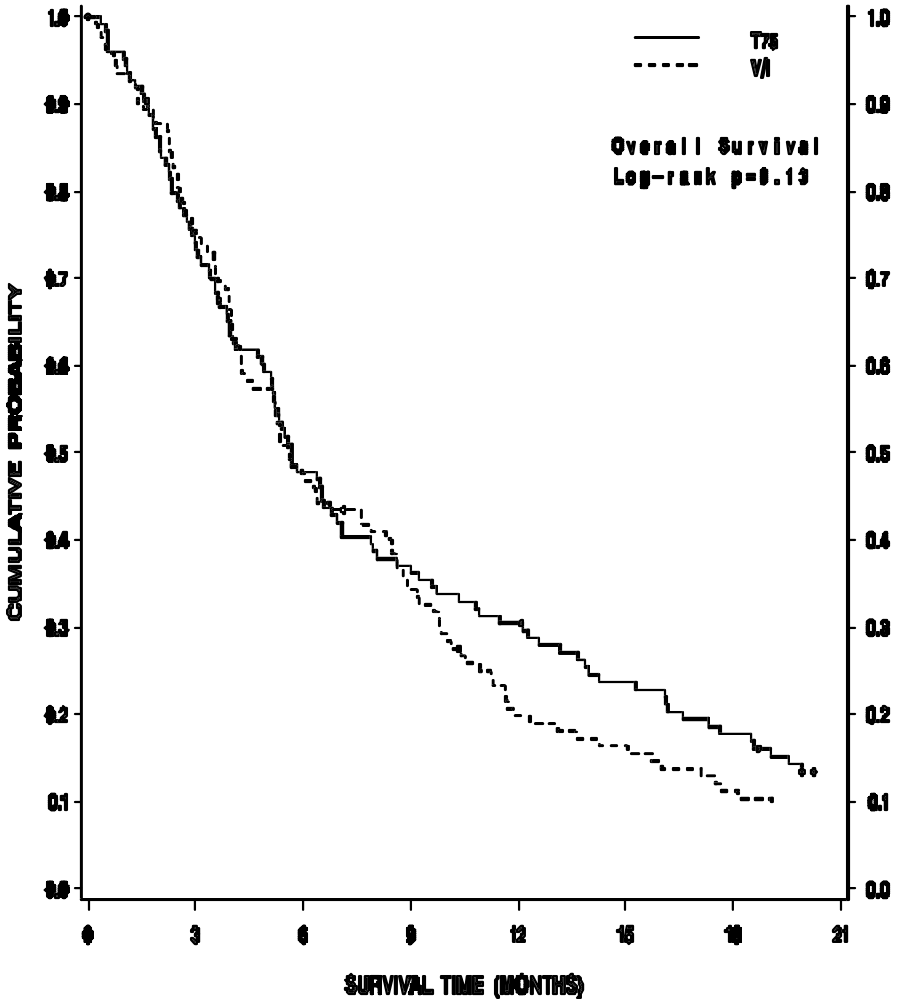
* $p \leq 0.05$; [@] uncorrected for multiple comparisons; [#] a value less than 1.00 favors docetaxel.

Only one of the two trials (TAX317) showed a clear effect on survival, the primary endpoint; that trial also showed an increased rate of survival to one year. In the second study (TAX320) the rate of survival at one year favored TAXOTERE 75 mg/m^2.

TAX 317 Survival K-M Curves - Docetaxel 75 mg/m^2 Vs. Best Supportive Care



TAX 320 Survival K-M Curves - Docetaxel 75 mg/m^2 Vs. Vinorelbine or Ifosfamide Control



Patients treated with TAXOTERE at a dose of 75mg/m^2 experienced no deterioration in performance status and body weight relative to the comparator arms used in these trials.

INDICATIONS AND USAGE

Breast Cancer: TAXOTERE® (docetaxel) for Injection Concentrate is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.

Non-Small Cell Lung Cancer: TAXOTERE® (docetaxel) for Injection Concentrate is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior platinum-based chemotherapy.

CONTRAINDICATIONS

TAXOTERE is contraindicated in patients who have a history of severe hypersensitivity reactions to docetaxel or to other drugs formulated with polysorbate 80.

TAXOTERE should not be used in patients with neutrophil counts of <1500 cells/mm^3.

WARNINGS

TAXOTERE (docetaxel) for Injection Concentrate should be administered under the supervision of a qualified physician experienced in the use of antineoplastic agents. Appropriate management of complications is possible only when adequate diagnostic and treatment facilities are readily available.

Toxic Deaths: Breast Cancer: TAXOTERE administered at 100 mg/m^2 was associated with deaths considered possibly or probably related to treatment in 2.0% (19/965) of metastatic breast cancer patients, both previously treated and untreated, with normal baseline liver function and in 11.5% (7/61) of patients with various tumor types who had abnormal baseline liver function (SGOT and/or SGPT > 1.5 times ULN together with AP > 2.5 times ULN). Among patients dosed at 60 mg/m^2, mortality related to treatment occurred in 0.6% (3/481) of patients with normal liver function, and in 3 of 7 patients with abnormal liver function. Approximately half of these deaths occurred during the first cycle. Sepsis accounted for the majority of the deaths.

Non-Small Cell Lung Cancer: TAXOTERE administered at a dose of 100 mg/m^2 in patients with locally advanced or metastatic non-small cell lung cancer who had a history of prior platinum-based chemotherapy was associated with increased treatment-related mortality (14% and 5% in two randomized, controlled studies). There were 2.8% treatment-related deaths among the 176 patients treated at the 75 mg/m^2 dose in the randomized trials. Among patients who experienced treatment-related mortality at the 75 mg/m^2 dose level, 3 of 5 patients had a PS of 2 at study entry. See BOXED WARNING, CLINICAL STUDIES, and DOSAGE AND ADMINISTRATION sections).

Premedication Regimen: All patients should be premedicated with oral corticosteroids such as dexamethasone 16 mg per day (*e.g.*, 8 mg BID) for 3 days starting 1 day prior to TAXOTERE to reduce the severity of fluid retention and hypersensitivity reactions (see **DOSAGE AND ADMINISTRATION** section). This regimen was evaluated in 92 patients with metastatic breast cancer previously treated with chemotherapy given TAXOTERE at a dose of 100 mg/m^2 every 3 weeks.

Hypersensitivity Reactions: Patients should be observed closely for hypersensitivity reactions, especially during the first and second infusions. Severe hypersensitivity reactions characterized by hypotension and/or bronchospasm, or generalized rash/erythema occurred in 2.2% of the 92 patients premedicated with 3-day corticosteroids. Hypersensitivity reactions requiring discontinuation of the TAXOTERE infusion were reported in 5 out of 1260 patients with various tumor types who did not receive premedication, but in 0/92 patients premedicated with
3-day corticosteroids. Patients with a history of severe hypersensitivity reactions should not be rechallenged with TAXOTERE.

Hematologic Effects: Neutropenia (< 2000 neutrophils/mm^3) occurs in virtually all patients given 60-100 mg/m^2 of TAXOTERE and grade 4 neutropenia (< 500 cells/mm^3) occurs in 85% of patients given 100 mg/m^2 and 75% of patients given 60 mg/m^2. Frequent monitoring of blood counts is, therefore, essential so that dose can be adjusted. TAXOTERE should not be administered to patients with neutrophils < 1500 cells/mm^3.

Febrile neutropenia occurred in about 12% of patients given 100 mg/m^2 but was very uncommon in patients given 60 mg/m^2. Hematologic responses, febrile reactions and infections, and rates of septic death for different regimens are dose related and are described in **CLINICAL STUDIES**.

Three breast cancer patients with severe liver impairment (bilirubin > 1.7 times ULN) developed fatal gastrointestinal bleeding associated with severe drug-induced thrombocytopenia.

Hepatic Impairment: (see **BOXED WARNING)**.

Fluid Retention: (see **BOXED WARNING)**.

Pregnancy: TAXOTERE can cause fetal harm when administered to pregnant women. Studies in both rats and rabbits at doses ≥ 0.3 and 0.03 mg/kg/day, respectively (about 1Ú50 and 1Ú300 the daily maximum recommended human dose on a mg/m^2 basis), administered during the period of organogenesis, have shown that TAXOTERE is embryotoxic and fetotoxic (characterized by intrauterine mortality, increased resorption, reduced fetal weight, and fetal ossification delay). The doses indicated above also caused maternal toxicity.

There are no adequate and well-controlled studies in pregnant women using TAXOTERE. If TAXOTERE is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus or potential risk for loss of the pregnancy. Women of childbearing potential should be advised to avoid becoming pregnant during therapy with TAXOTERE.

PRECAUTIONS

General: Responding patients may not experience an improvement in performance status on therapy and may experience worsening. The relationship between changes in performance status, response to therapy, and treatment-related side effects has not been established.

Hematologic Effects: In order to monitor the occurrence of myelotoxicity, it is recommended that frequent peripheral blood cell counts be performed on all patients receiving TAXOTERE. Patients should not be retreated with subsequent cycles of TAXOTERE until neutrophils recover to a level > 1500 cells/mm^3 and platelets recover to a level > 100,000 cells/mm^3.

A 25% reduction in the dose of TAXOTERE is recommended during subsequent cycles following severe neutropenia (< 500 cells/mm^3) lasting 7 days or more, febrile neutropenia, or a grade 4 infection in a TAXOTERE® (docetaxel) for Injection Concentrate cycle (see **DOSAGE AND ADMINISTRATION** section).

Hypersensitivity Reactions: Hypersensitivity reactions may occur within a few minutes following initiation of a TAXOTERE infusion. If minor reactions such as flushing or localized skin reactions occur, interruption of therapy is not required. More severe reactions, however, require the immediate discontinuation of TAXOTERE and aggressive therapy. All patients should be premedicated with an oral corticosteroid prior to the initiation of the infusion of TAXOTERE (see **BOXED WARNING** and **WARNINGS**: **Premedication Regimen**).

Cutaneous: Localized erythema of the extremities with edema followed by desquamation has been observed. In case of severe skin toxicity, an adjustment in dosage is recommended (see **DOSAGE AND ADMINISTRATION** section). The discontinuation rate due to skin toxicity was 1.6% (15/965) for metastatic breast cancer patients. Among 92 breast cancer patients premedicated with 3-day corticosteroids, there were no cases of severe skin toxicity reported and no patient discontinued TAXOTERE due to skin toxicity.

Fluid Retention: Severe fluid retention has been reported following TAXOTERE therapy (see **BOXED WARNING** and **WARNINGS**: **Premedication Regimen**). Patients should be premedicated with oral corticosteroids prior to each TAXOTERE administration to reduce the incidence and severity of fluid retention (see **DOSAGE AND ADMINISTRATION** section). Patients with pre-existing effusions should be closely monitored from the first dose for the possible exacerbation of the effusions.

When fluid retention occurs, peripheral edema usually starts in the lower extremities and may become generalized with a median weight gain of 2 kg.

Among 92 breast cancer patients premedicated with 3-day corticosteroids, moderate fluid retention occurred in 27.2% and severe fluid retention in 6.5%. The median cumulative dose to onset of moderate or severe fluid retention was 819 mg/m^2.

9.8% (9/92) of patients discontinued treatment due to fluid retention: 4 patients discontinued with severe fluid retention; the remaining 5 had mild or moderate fluid retention. The median cumulative dose to treatment discontinuation due to fluid retention was 1021 mg/m^2. Fluid retention was completely, but sometimes slowly, reversible with a median of 16 weeks from the last infusion of TAXOTERE to resolution (range: 0 to 42+ weeks). Patients developing peripheral edema may be treated with standard measures, *e.g.*, salt restriction, oral diuretic(s).

Neurologic: Severe neurosensory symptoms (paresthesia, dysesthesia, pain) were observed in 5.5% (53/965) of metastatic breast cancer patients, and resulted in treatment discontinuation in 6.1%. When these symptoms occur, dosage must be adjusted. If symptoms persist, treatment should be discontinued (see **DOSAGE AND ADMINISTRATION** section). Patients who experienced neurotoxicity in clinical trials and for whom follow-up information on the complete resolution of the event was available had spontaneous reversal of symptoms with a median of 9 weeks from onset (range: 0 to 106 weeks). Severe peripheral motor neuropathy mainly manifested as distal extremity weakness occurred in 4.4% (42/965).

Asthenia: Severe asthenia has been reported in 14.9% (144/965) of metastatic breast cancer patients but has led to treatment discontinuation in only 1.8%. Symptoms of fatigue

and weakness may last a few days up to several weeks and may be associated with deterioration of performance status in patients with progressive disease.

Information for Patients: For additional information, see the accompanying Patient Information Leaflet.

Drug Interactions: There have been no formal clinical studies to evaluate the drug interactions of TAXOTERE with other medications. *In vitro* studies have shown that the metabolism of docetaxel may be modified by the concomitant administration of compounds that induce, inhibit, or are metabolized by cytochrome P450 3A4, such as cyclosporine, terfenadine, ketoconazole, erythromycin, and troleandomycin. Caution should be exercised with these drugs when treating patients receiving TAXOTERE as there is a potential for a significant interaction.

Carcinogenicity, Mutagenicity, Impairment of Fertility: No studies have been conducted to assess the carcinogenic potential of TAXOTERE. TAXOTERE has been shown to be clastogenic in the *in vitro* chromosome aberration test in CHO-K_1 cells and in the *in vivo* micronucleus test in the mouse, but it did not induce mutagenicity in the Ames test or the CHO/HGPRT gene mutation assays. TAXOTERE produced no impairment of fertility in rats when administered in multiple IV doses of up to 0.3 mg/kg (about 1Ú50 the recommended human dose on a mg/m^2 basis), but decreased testicular weights were reported. This correlates with findings of a 10-cycle toxicity study (dosing once every 21 days for 6 months) in rats and dogs in which testicular atrophy or degeneration was observed at IV doses of 5 mg/kg in rats and 0.375 mg/kg in dogs (about 1Ú3 and 1Ú15 the recommended human dose on a mg/m^2 basis, respectively). An increased frequency of dosing in rats produced similar effects at lower dose levels.

Pregnancy: Pregnancy Category D (see **WARNINGS** section).

Nursing Mothers: It is not known whether TAXOTERE is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from TAXOTERE, mothers should discontinue nursing prior to taking the drug.

Pediatric Use: The safety and effectiveness of TAXOTERE in pediatric patients have not been established.

ADVERSE REACTIONS

The adverse reactions are described separately for TAXOTERE 100 mg/m^2, the maximum dose approved for breast cancer, and 75 mg/m^2, the dose approved for advanced non-small cell lung carcinoma after prior platinum-based chemotherapy.

TAXOTERE 100 mg/m^2: Adverse drug reactions occurring in at least 5% of patients are compared for three populations who received TAXOTERE administered at 100 mg/m^2 as a 1-hour infusion every 3 weeks: 2045 patients with various tumor types and normal baseline liver function tests; the subset of 965 patients with locally advanced or metastatic breast cancer, both previously treated and untreated with chemotherapy, who had normal baseline liver function tests; and an additional 61 patients with various tumor types who had

abnormal liver function tests at baseline. These reactions were described using COSTART terms and were considered possibly or probably related to TAXOTERE. At least 95% of these patients did not receive hematopoietic support. The safety profile is generally similar in patients receiving TAXOTERE for the treatment of breast cancer and in patients with other tumor types.

Summary of Adverse Events in Patients Receiving TAXOTERE at 100 mg/m^2

Adverse Event	All Tumor Types Normal LFTs* n=2045 %	All Tumor Types Elevated LFTs** n=61 %	Breast Cancer Normal LFTs* n=965 %
Hematologic			
Neutropenia			
<2000 cells/mm^3	95.5	96.4	98.5
<500 cells/mm^3	75.4	87.5	85.9
Leukopenia			
<4000 cells/mm^3	95.6	98.3	98.6
<1000 cells/mm^3	31.6	46.6	43.7
Thrombocytopenia			
<100,000 cells/mm^3	8.0	24.6	9.2
Anemia			
<11 g/dL	90.4	91.8	93.6
<8 g/dL	8.8	31.1	7.7
Febrile Neutropenia***	11.0	26.2	12.3
Septic Death	1.6	4.9	1.4
Non-Septic Death	0.6	6.6	0.6
Infections			
Any	21.6	32.8	22.2
Severe	6.1	16.4	6.4
Fever in Absence of Infection			
Any	31.2	41.0	35.1
Severe	2.1	8.2	2.2
Hypersensitivity Reactions			
Regardless of Premedication			
Any	21.0	19.7	17.6
Severe	4.2	9.8	2.6
With 3-day Premedication	n=92	n=3	n=92
Any	15.2	33.3	15.2
Severe	2.2	0	2.2
Fluid Retention			

Regardless of Premedication			
Any	47.0	39.3	59.7
Severe	6.9	8.2	8.9
With 3-day Premedication	n=92	n=3	n=92
Any	64.1	66.7	64.1
Severe	6.5	33.3	6.5
Neurosensory			
Any	49.3	34.4	58.3
Severe	4.3	0	5.5
Cutaneous			
Any	47.6	54.1	47.0
Severe	4.8	9.8	5.2
Nail Changes			
Any	30.6	23.0	40.5
Severe	2.5	4.9	3.7
Gastrointestinal			
Nausea	38.8	37.7	42.1
Vomiting	22.3	23.0	23.4
Diarrhea	38.7	32.8	42.6
Severe	4.7	4.9	5.5
Stomatitis			
Any	41.7	49.2	51.7
Severe	5.5	13.0	7.4
Alopecia	75.8	62.3	74.2
Asthenia			
Any	61.8	52.5	66.3
Severe	12.8	24.6	14.9
Myalgia			
Any	18.9	16.4	21.1
Severe	1.5	1.6	1.8
Arthralgia	9.2	6.6	8.2
Infusion Site Reactions	4.4	3.3	4.0

***Normal Baseline LFTs: Transaminases ≤ 1.5 times ULN or alkaline phosphatase ≤ 2.5 times ULN or isolated elevations of transaminases or alkaline phosphatase up to 5 times ULN**

****Elevated Baseline LFTs: SGOT and/or SGPT > 1.5 times ULN concurrent with alkaline phosphatase > 2.5 times ULN**

***Febrile Neutropenia: ANC grade 4 with fever > 38°C with IV antibiotics and/or hospitalization

Hematologic: (see **WARNINGS)**. Reversible marrow suppression was the major dose-limiting toxicity of TAXOTERE. The median time to nadir was 7 days, while the median duration of severe neutropenia (<500 cells/mm^3) was 7 days. Among

2045 patients with solid tumors and normal baseline LFTs, severe neutropenia occurred in 75.4% and lasted for more than 7 days in 2.9% of cycles.

Febrile neutropenia (<500 cells/mm^3 with fever > 38°C with IV antibiotics and/or hospitalization) occurred in 11% of patients with solid tumors, in 12.3% of patients with metastatic breast cancer, and in 9.8% of 92 breast cancer patients premedicated with 3-day corticosteroids.

Severe infectious episodes occurred in 6.1% of patients with solid tumors, in 6.4% of patients with metastatic breast cancer, and in 5.4% of 92 breast cancer patients premedicated with 3-day corticosteroids.

Thrombocytopenia (<100,000 cells/mm^3) associated with fatal gastrointestinal hemorrhage has been reported.

Hypersensitivity Reactions: Severe hypersensitivity reactions are discussed in the **BOXED WARNING, WARNINGS,** and **PRECAUTIONS** sections. Minor events, including flushing, rash with or without pruritus, chest tightness, back pain, dyspnea, drug fever, or chills, have been reported and resolved after discontinuing the infusion and appropriate therapy.

Fluid Retention: (see **BOXED WARNING**, **WARNINGS: Premedication Regimen**, and **PRECAUTIONS** sections**)**.

Cutaneous: Severe skin toxicity is discussed in **PRECAUTIONS**. Reversible cutaneous reactions characterized by a rash including localized eruptions, mainly on the feet and/or hands, but also on the arms, face, or thorax, usually associated with pruritus, have been observed. Eruptions generally occurred within 1 week after TAXOTERE infusion, recovered before the next infusion, and were not disabling.

Severe nail disorders were characterized by hypo- or hyperpigmentation, and occasionally by onycholysis (in 0.8% of patients with solid tumors) and pain.

Neurologic: **(**see **PRECAUTIONS)**.

Gastrointestinal: Gastrointestinal reactions (nausea and/or vomiting and/or diarrhea) were generally mild to moderate. Severe reactions occurred in 3-5% of patients with solid tumors and to a similar extent among metastatic breast cancer patients. The incidence of severe reactions was 1% or less for the 92 breast cancer patients premedicated with 3-day corticosteroids.

Severe stomatitis occurred in 5.5% of patients with solid tumors, in 7.4% of patients with metastatic breast cancer, and in 1.1% of the 92 breast cancer patients premedicated with 3-day corticosteroids.

Cardiovascular: Hypotension occurred in 2.8% of patients with solid tumors; 1.2% required treatment. Clinically meaningful events such as heart failure, sinus tachycardia, atrial

flutter, dysrhythmia, unstable angina, pulmonary edema, and hypertension occurred rarely. 8.1% (7/86) of metastatic breast cancer patients receiving TAXOTERE 100 mg/m^2 in a randomized trial and who had serial left ventricular ejection fractions assessed developed deterioration of LVEF by ≥ 10% associated with a drop below the institutional lower limit of normal.

Infusion Site Reactions: Infusion site reactions were generally mild and consisted of hyperpigmentation, inflammation, redness or dryness of the skin, phlebitis, extravasation, or swelling of the vein.

Hepatic: In patients with normal LFTs at baseline, bilirubin values greater than the ULN occurred in 8.9% of patients. Increases in SGOT or SGPT > 1.5 times the ULN, or alkaline phosphatase > 2.5 times ULN, were observed in 18.9% and 7.3% of patients, respectively. While on TAXOTERE, increases in SGOT and/or SGPT > 1.5 times ULN concomitant with alkaline phosphatase > 2.5 times ULN occurred in 4.3% of patients with normal LFTs at baseline. (Whether these changes were related to the drug or underlying disease has not been established.)

TAXOTERE 75 mg/m^2: Treatment emergent adverse drug reactions are shown below. Included in this table are safety data for a total of 176 patients with non-small cell lung carcinoma and a history of prior treatment with platinum-based chemotherapy who were treated in two randomized, controlled trials. These reactions were described using NCI Common Toxicity Criteria regardless of relationship to study treatment, except for the hematologic toxicities or otherwise noted.

Treatment Emergent Adverse Events in Non-Small Cell Lung Cancer Patients Receiving Taxotere Regardless of Relationship to Treatment*

Adverse Event	TAXOTERE 75 mg/m^2 N=176 (%)	Best Supportive Care N=49 (%)	Vinorelbine/Ifosfamide N=119 (%)
Neutropenia			
Any	148 (85.5)	7 (16.3)	99 (85.3)
Grade 3/4	115 (66.5)	6 (14.0)	68 (58.6)
Leukopenia			
Any	147 (85.0)	3 (6.8)	106 (91.4)
Grade ¾	87 (50.0)	0	51 (44.0)
Thrombocytopenia			
Any	14 (8.0)	0	9 (7.7)
Grade 3/4	5 (2.9)	0	2 (1.7)
Anemia			
Any	160 (91.4)	27 (61.4)	108 (92.3)
Grade 3/4	16 (9.1)	6 (13.6)	17 (14.5)
Febrile Neutropenia**	11 (6.3)	NA$^{\xi}$	1 (0.8)
Infection			
Any	59 (33.5)	14 (28.6)	36 (30.3)
Grade 3/4	18 (10.2)	3 (6.1)	11 (9.2)
Treatment Related Mortality	5 (2.8)	NA$^{\xi}$	4 (3.4)
Hypersensitivity Reactions			
Any	10 (5.7)	0	1 (0.8)
Grade 3/4	5 (2.8)	0	0
Fluid Retention			
Any	59 (33.5)	ND$^{\Psi}$	27 (22.7)
Severe	5 (2.8)		4 (3.4)
Neurosensory			
Any	41 (23.3)	7 (14.3)	34 (28.6)
Grade 3/4	3 (1.7)	3 (6.1)	6 (5.0)

Neuromotor			
Any	28 (15.9)	4 (8.2)	12 (10.1)
Grade 3/4	8 (4.5)	3 (6.1)	4 (3.4)
Skin			
Any	35 (19.8)	3 (6.1)	20 (16.8)
Grade 3/4	1 (0.6)	1 (2.0)	1 (0.8)
Gastrointestinal			
Nausea			
Any	59 (33.5)	15 (30.6)	37 (31.1)
Grade 3/4	9 (5.1)	2 (4.1)	9 (7.6)
Vomiting			
Any	38 (21.6)	13 (26.5)	26 (21.8)
Grade 3/4	5 (2.8)	1 (2.0)	7 (5.9)
Diarrhea			
Any	40 (22.7)	3 (6.1)	14 (11.8)
Grade 3/4	5 (2.8)	0	5 (4.2)

Alopecia	99 (56.3)	17 (34.7)	59 (49.6)
Asthenia			
Any	93 (52.8)	28 (57.1)	64 (53.8)
Severe***	32 (18.2)	19 (38.8)	27 (22.7)
Stomatitis			
Any	46 (26.1)	3 (6.1)	9 (7.6)
Grade 3/4	3 (1.7)	0	1 (0.8)
Pulmonary			
Any	72 (40.9)	24 (49.0)	54 (45.4)
Grade 3/4	37 (21.0)	14 (28.6)	22 (18.5)
Nail Disorder			
Any	20 (11.4)	0	2 (1.7)
Severe***	2 (1.1)	0	0
Myalgia			
Any	11 (6.3)	0	3 (2.5)
Severe***	0	0	0
Arthralgia			
Any	6 (3.4)	1 (2.0)	2 (1.7)
Severe***	0	0	1 (0.8)
Taste Perversion			
Any	10 (5.7)	0	0
Severe***	1 (0.6)	0	0

***Normal Baseline LFTs: Transaminases ≤ 1.5 times ULN or alkaline phosphatase ≤ 2.5 times ULN or isolated elevations of transaminases or alkaline phosphatase up to 5 times ULN**

****Febrile Neutropenia: ANC grade 4 with fever > 38°C with IV antibiotics and/or hospitalization**

*** COSTART term and grading system

ξ **Not Applicable;** ψ Not Done

Ongoing Evaluation: The following serious adverse events of uncertain relationship to TAXOTERE have been reported:

Body as a whole: abdominal pain, diffuse pain, chest pain, radiation recall phenomenon

Cardiovascular: atrial fibrillation, deep vein thrombosis, ECG abnormalities, thrombophlebitis, pulmonary embolism, syncope, tachycardia, myocardial infarction

Digestive: constipation, duodenal ulcer, esophagitis, gastrointestinal hemorrhage, intestinal obstruction, ileus, gastrointestinal perforation, neutropenic enterocolitis, dehydration in relation to digestive disorders

Nervous: confusion, seizures

Respiratory: dyspnea, acute pulmonary edema, acute respiratory distress syndrome, interstitial pneumonia

Urogenital: renal insufficiency

OVERDOSAGE

There is no known antidote for TAXOTERE overdosage. In case of overdosage, the patient should be kept in a specialized unit where vital functions can be closely monitored. Anticipated complications of overdosage include: bone marrow suppression, peripheral neurotoxicity, and mucositis. Patients should receive therapeutic G-CSF as soon as possible after discovery of overdose. Other appropriate symptomatic measures should be taken, as needed.

In two reports of overdose, one patient received 150 mg/m^2 and the other received 200 mg/m^2 as 1-hour infusions. Both patients experienced severe neutropenia, mild asthenia, cutaneous reactions, and mild paresthesia, and recovered without incident.

In mice, lethality was observed following single IV doses that were ≥154 mg/kg (about 4.5 times the recommended human dose on a mg/m^2 basis); neurotoxicity associated with paralysis, non-extension of hind limbs, and myelin degeneration was observed in mice at 48 mg/kg (about 1.5 times the recommended human dose on a mg/m^2 basis). In male and female rats, lethality was observed at a dose of 20 mg/kg (comparable to the recommended human dose on a mg/m^2 basis) and was associated with abnormal mitosis and necrosis of multiple organs.

DOSAGE AND ADMINISTRATION

Breast Cancer: The recommended dose of TAXOTERE is 60-100 mg/m^2 administered intravenously over 1 hour every 3 weeks.

Non Small Cell Lung Cancer: The recommended dose of TAXOTERE is 75 mg/m^2 administered intravenously over 1 hour every 3 weeks. A dose of 100 mg/m^2 in patients previously treated with chemotherapy was associated with increased hematologic toxicity, infection, and treatment-related mortality in randomized, controlled trials (see BOXED WARNING, WARNINGS and CLINICAL STUDIES sections).

Premedication Regimen: All patients should be premedicated with oral corticosteroids such as dexamethasone 16 mg per day (*e.g.*, 8 mg BID) for 3 days starting 1 day prior to TAXOTERE administration in order to reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions
(see **BOXED WARNING**, **WARNINGS,** and **PRECAUTIONS** sections).

Dosage Adjustments During Treatment:

Breast Cancer. Patients who are dosed initially at 100 mg/m^2 and who experience either febrile neutropenia, neutrophils < 500 cells/mm^3 for more than 1 week, or severe or cumulative cutaneous reactions during TAXOTERE therapy should have the dosage adjusted from 100 mg/m^2 to 75 mg/m^2. If the patient continues to experience these reactions, the dosage should either be decreased from 75 mg/m^2 to 55 mg/m^2 or the treatment should be discontinued. Conversely, patients who are dosed initially at 60 mg/m^2 and who do not experience febrile neutropenia, neutrophils <500 cells/mm^3 for more than 1 week, severe or cumulative cutaneous reactions, or severe peripheral neuropathy during TAXOTERE therapy may tolerate higher doses. Patients who develop ≥ grade 3 peripheral neuropathy should have TAXOTERE treatment discontinued entirely.

Non-Small Cell Lung Cancer. Patients who are dosed initially at 75 mg/m^2 and who experience either febrile neutropenia, neutrophils <500 cells/mm^3 for more than one week, severe or cumulative cutaneous reactions, or other grade ¾ non-hematological toxicities during TAXOTERE treatment should have treatment withheld until resolution of the toxicity and then resumed at 55 mg/m^2. Patients who develop ≥ grade 3 peripheral neuropathy should have TAXOTERE treatment discontinued entirely.

Special Populations:

Hepatic Impairment: Patients with bilirubin > ULN should generally not receive TAXOTERE. Also, patients with SGOT and/or SGPT > 1.5 x ULN concomitant with alkaline phosphatase > 2.5 x ULN should generally not receive TAXOTERE.

Children: The safety and effectiveness of docetaxel in pediatric patients below the age of 16 years have not been established.

Elderly: No dosage adjustments are required for use in elderly.

PREPARATION AND ADMINISTRATION PRECAUTIONS[a]

TAXOTERE is a cytotoxic anticancer drug and, as with other potentially toxic compounds, caution should be exercised when handling and preparing TAXOTERE solutions. The use of gloves is recommended. Please refer to **Handling and Disposal** section.

[a] FDA fax 09 August 1999

If TAXOTERE concentrate, initial diluted solution, or final dilution for infusion should come into contact with the skin, immediately and thoroughly wash with soap and water. If TAXOTERE concentrate, initial diluted solution, or final dilution for infusion should come into contact with mucosa, immediately and thoroughly wash with water.

TAXOTERE for Injection Concentrate requires two dilutions prior to administration. Please follow the preparation instructions provided below. **Note:** Both the TAXOTERE for Injection Concentrate and the diluent vials contain an overfill.

A. Preparation of the Initial Diluted Solution

1. Remove the appropriate number of vials of TAXOTERE for Injection Concentrate and diluent (13% Ethanol in Water for Injection) from the refrigerator. Allow the vials to stand at room temperature for approximately 5 minutes.

2. Aseptically withdraw the contents of the appropriate diluent vial into a syringe and transfer it to the appropriate vial of TAXOTERE for Injection Concentrate. **If the procedure is followed as described, an initial diluted solution of 10mg docetaxel/mL will result.**

3. Gently rotate the initial diluted solution for approximately 15 seconds to assure full mixture of the concentrate and diluent.

4. The initial diluted TAXOTERE solution (10 mg docetaxel/mL) should be clear; however, there may be some foam on top of the solution due to the polysorbate 80. Allow the solution to stand for a few minutes to allow any foam to dissipate. It is not required that all foam dissipate prior to continuing the preparation process.

B. Preparation of the Final Dilution for Infusion

1. Aseptically withdraw the required amount of initial diluted TAXOTERE solution (10 mg docetaxel/mL) with a calibrated syringe and inject into a 250 mL infusion bag or bottle of either 0.9% Sodium Chloride solution or 5% Dextrose solution to produce a final concentration of 0.3 to 0.9 mg/mL.

   If a dose greater than 240 mg of TAXOTERE is required, use a larger volume of the infusion vehicle so that a concentration of 0.9 mg/mL TAXOTERE is not exceeded.

2. Thoroughly mix the infusion by manual rotation.

3. As with all parenteral products, TAXOTERE should be inspected visually for particulate matter or discoloration prior to administration whenever the solution and container permit. If the TAXOTERE for Injection initial diluted solution or final dilution for infusion is not clear or appears to have precipitation, these should be discarded.

The final TAXOTERE dilution for infusion should be administered intravenously as a 1-hour infusion under ambient room temperature and lighting conditions.

Contact of the TAXOTERE concentrate with plasticized PVC equipment or devices used to prepare solutions for infusion is not recommended. In order to minimize patient exposure to the plasticizer DEHP (di-2-ethylhexyl phthalate), which may be leached from PVC infusion bags or sets, the final TAXOTERE dilution for infusion should be stored in bottles (glass, polypropylene) or plastic bags (polypropylene, polyolefin) and administered through polyethylene-lined administration sets.

Stability: Unopened vials of TAXOTERE are stable until the expiration date indicated on the package when stored refrigerated, 2° to 8°C (36° to 46°F), and protected from bright light. Freezing does not adversely affect the product.

HOW SUPPLIED

TAXOTERE for Injection Concentrate is supplied in a single-dose vial as a sterile, pyrogen-free, non-aqueous, viscous solution with an accompanying sterile, non-pyrogenic, diluent (13% ethanol in Water for Injection) vial. The following strengths are available:

TAXOTERE 80 MG (NDC 0075-8001-80)

TAXOTERE (docetaxel) 80 mg Concentrate for Infusion: 80 mg docetaxel in 2 mL polysorbate 80 diluent for TAXOTERE 80 mg. 13% (w/w) ethanol in Water for Injection . Both items are in a blister pack in one carton.

TAXOTERE 20 MG (NDC 0075-8001-20)

TAXOTERE (docetaxel) 20 mg Concentrate for Infusion: 20 mg docetaxel in 0.5 mL polysorbate 80 and diluent for TAXOTERE 20 mg. 13% (w/w) ethanol in Water for Injection . Both items are in a blister pack in one carton.

Storage: Store refrigerated, 2° to 8°C (36° to 46°F). Retain in the original package to protect from bright light.

TAXOTERE premix solution (10 mg TAXOTERE/mL) and fully prepared TAXOTERE infusion solution (in either 0.9% Sodium Chloride solution or 5% Dextrose solution) should be used as soon as possible after preparation. However, the premix solution is stable for 8 hours either at room temperature, 15° to 25°C
(59° to 77°F), or stored refrigerated, 2° to 8°C (36° to 46°F).

Handling and Disposal: Procedures for proper handling and disposal of anticancer drugs should be considered. Several guidelines on this subject have been published[1-8]. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate.

REFERENCES

1. OSHA Work-Practice Guidelines for Personnel Dealing with Cytotoxic (Antineoplastic) Drugs. *Am J Hosp Pharm.* 1986; 43(5): 1193-1204
2. American Society of Hospital Pharmacists Technical Assistance Bulletin on Handling Cytotoxic and Hazardous Drugs. *Am J Hosp Pharm.* 1990; 47(95): 1033-1049.
3. AMA Council Report. Guidelines for Handling Parenteral Antineoplastics. *JAMA* 1985; 253 (11): 1590-1592.
4. Oncology Nursing Society Clinical Practice Committee. Cancer Chemotherapy Guidelines. Module II – Recommendations of Nursing Practice in the Acute Care Setting. *ONS* 1988; 2-14.
5. Recommendations for the Safe Handling of Parenteral Antineoplastic Drugs. NIH Publication No. 83-2621. For sale by the Superintendent of Documents, US Government Printing Office, Washington, DC 20402.

6. National Study Commission on Cytotoxic Exposure - Recommendations for Handling Cytotoxic Agents. Available from Louis P. Jeffry, Chairman, National Study Commission on Cytotoxic Exposure. Massachusetts College of Pharmacy and Allied Health Sciences, 179 Longwood Avenue, Boston, MA 02115.
7. Clinical Oncological Society of Australia. Guidelines and Recommendations for Safe Handling of Antineoplastic Agents. *Med J Austr*. 1983; 426-428.
8. Jones, RB, et al. Safe Handling of Chemotherapeutic Agents: A Report from the Mt. Sinai Medical Center. *CA-A Cancer Journal for Clinicians* 1983; Sept/Oct: 258-263.

RHÔNE-POULENC RORER PHARMACEUTICALS INC.
COLLEGEVILLE, PA 19426

IN-5493D Rev. 7/98

Patient Information Leaflet
Detach and give to Patient

IN-5493D
Rev. 7/98

Patient Information Leaflet

Questions and Answers About Taxotere® for Injection Concentrate

(generic name = docetaxel)

(pronounced as TAX-O-TEER)

What is Taxotere?

Taxotere is a medication to treat breast cancer and non-small cell lung cancer. It has severe side effects in some patients. This leaflet is designed to help you understand how to use Taxotere and avoid its side effects to the fullest extent possible. The more you understand your treatment, the better you will be able to participate in your care. If you have questions or concerns, be sure to ask your doctor or nurse. They are always your best source of information about your condition and treatment.

What is the most important information about Taxotere?

- Since this drug, like many other cancer drugs, affects your blood cells, your doctor will ask for routine blood tests. These will include regular checks of your white blood cell counts. About 5% of people with low blood counts have developed life-threatening infections. The earliest sign of infection may be fever, so if you experience a fever, tell your doctor right away.
- Occasionally, serious allergic reactions have occurred with this medicine. If you have any allergies, tell your doctor before receiving this medicine.
- A small number of people who take Taxotere have severe fluid retention, which can be life-threatening. To help avoid this problem, you must take another medication called dexamethasone (DECKS-A-METH-A-SONE) prior to each Taxotere treatment. You must follow the schedule and take the exact dose of dexamethasone prescribed (see schedule at end of brochure). If you forget to take a dose or do not take it on schedule you must tell the doctor or nurse prior to your Taxotere treatment.
- If you are using any other medicines, tell your doctor before receiving your infusions of Taxotere.

How does Taxotere work?

Taxotere works by attacking cancer cells in your body. Different cancer medications attack cancer cells in different ways.

Here's how Taxotere works: Every cell in your body contains a supporting structure (like a skeleton). If this "skeleton" is damaged, it cannot grow or reproduce. Taxotere makes the "skeleton" in cancer cells very stiff, so that the cells can no longer grow.

How will I receive Taxotere?

Taxotere is given by an infusion directly into your vein. Your treatment will take about 1 hour. Generally, people receive Taxotere every 3 weeks. The amount of Taxotere and the frequency of your infusions will be determined by your doctor.

As part of your treatment, to reduce side effects your doctor will prescribe another medicine called dexamethasone. Your doctor will tell you how and when to take this medicine. It is important that you take the dexamethasone on the schedule set by your doctor. If you forget to take your medication, or do not take it on schedule, make sure to tell your doctor or nurse **BEFORE** you receive your Taxotere treatment. **Included with this information leaflet is a chart to help you remember when to take your dexamethasone.**

What should be avoided while receiving Taxotere?

Taxotere can interact with other medicines. Use only medicines that are prescribed for you by your doctor and **be sure** to tell your doctor all the medicines that you use, including nonprescription drugs.

What are the possible side effects of Taxotere?

Low Blood Cell Count – Many cancer medications, including Taxotere, cause a temporary drop in the number of white blood cells. These cells help protect your body from infection. Your doctor will routinely check your blood count and tell you if it is too low. Although most people receiving Taxotere do not have an infection even if they have a low white blood cell count, the risk of infection is increased.

Fever is often one of the most common and earliest signs of infection. Your doctor will recommend that you take your temperature frequently, especially during the days after treatment with Taxotere. If you have a fever, tell your doctor or nurse immediately.

Allergic Reactions – This type of reaction, which occurs during the infusion of Taxotere, is infrequent. If you feel a warm sensation, a tightness in your chest, or itching during or shortly after your treatment, tell your doctor or nurse immediately.

Fluid Retention – This means that your body is holding extra water. If this fluid retention is in the chest or around the heart it can be life-threatening. If you notice swelling in the feet and legs or a slight weight gain, this may be the first warning sign. Fluid retention usually does not start immediately; but, if it occurs, it may start around your 5th treatment. Generally, fluid retention will go away within weeks or months after your treatments are completed.

Dexamethasone tablets may protect patients from significant fluid retention. It is important that you take this medicine on schedule. If you have not taken dexamethasone on schedule, you must tell your doctor or nurse before receiving your next Taxotere treatment.

Hair Loss – Loss of hair occurs in most patients taking Taxotere (including the hair on your head, underarm hair, pubic hair, eyebrows, and eyelashes). Hair loss will begin after the first few treatments and varies from patient to patient. Once you have completed all your treatments, hair generally grows back.

Your doctor or nurse can refer you to a store that carries wigs, hairpieces, and turbans for patients with cancer.

Fatigue – A number of patients (about 10%) receiving Taxotere feel very tired following their treatments. If you feel tired or weak, allow yourself extra rest before your next treatment. If it is bothersome or lasts for longer than 1 week, inform your doctor or nurse.

Muscle Pain – This happens about 20% of the time, but is rarely severe. You may feel pain in your muscles or joints. Tell your doctor or nurse if this happens. They may suggest ways to make you more comfortable.

Rash – This side effect occurs commonly but is severe in about 5%. You may develop a rash that looks like a blotchy, hive-like reaction. This usually occurs on the hands and feet but may also appear on the arms, face, or body. Generally, it will appear between treatments and will go away before the next treatment. Inform your doctor or nurse if you experience a rash. They can help you avoid discomfort.

Odd Sensations – About half of patients getting Taxotere will feel numbness, tingling, or burning sensations in their hands and feet. If you do experience this, tell your doctor or nurse. Generally, these go away within a few weeks or months after your treatments are completed. About 14% of patients may also develop weakness in their hands and feet.

Nail Changes – Color changes to your fingernails or toenails may occur while taking Taxotere. In extreme, but rare, cases nails may fall off. After you have finished Taxotere treatments, your nails will generally grow back.

Other Possible Side Effects – Less severe side effects include nausea and vomiting. Severe diarrhea may occasionally occur. If you experience these or any other unusual effects, tell your doctor or nurse.

If you are interested in learning more about this drug, ask your doctor for a copy of the package insert.

IN-5493D Rev. 7/98

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COLLEGEVILLE, PA 19426

Date _____
Day 1

Start
Dexamethasone tablets
2 times per day
AM
PM

Date _____
Day 2

Taxotere
Treatment Day

Take
Dexamethasone tablets
2 times per day
AM
PM

Date _____
Day 3

Take
Dexamethasone tablets
2 times per day
AM
PM

UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF LOUISIANA

In Re: TAXOTERE (DOCETAXEL) PRODUCTS LIABILITY LITIGATION

MDL NO. 2740

SECTION "N" (5)

THIS DOCUMENT RELATES TO ALL CASES

NOTICE OF SUBMISSION

PLEASE TAKE NOTICE that Defendants, sanofi-aventis U.S. LLC, Sanofi US Services Inc., Sandoz Inc., Hospira, Inc., Hospira Worldwide, LLC, Pfizer Inc., Actavis Pharma, Inc., Accord Healthcare, Inc., Sun Pharma Global Inc.,[1] and McKesson Corporation will bring for hearing the accompanying Motion to Dismiss Plaintiffs' Master Long Form Complaint on the 30th day of August, 2017, at 9:30 a.m., before the Honorable Kurt D. Engelhardt of the United States District Court for the Eastern District of Louisiana, 500 Poydras Street, New Orleans, LA 70130.

[1] At the time of filing this Motion, Sun Pharma Global Inc. and Plaintiffs have agreed to a voluntary dismissal without prejudice and have further agreed to substitute and accept streamlined service of process for Sun Pharmaceutical Industries, Inc. f/k/a Caraco Laboratories, Ltd. Plaintiffs have also named Sun Pharma Global FZE in this litigation but Sun Pharma Global FZE is a foreign company incorporated under the laws of the United Arab Emirates and has not been served with process, has not agreed to accept service of process in this litigation and consequently, Sun Pharma Global FZE is not appearing in this matter or joining in this Motion.

Respectfully Submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on May 26, 2017, I electronically filed the foregoing with the Clerk of the Court using the ECF system which sent notification of such filing to all counsel of record.

/s/ *Douglas J. Moore*